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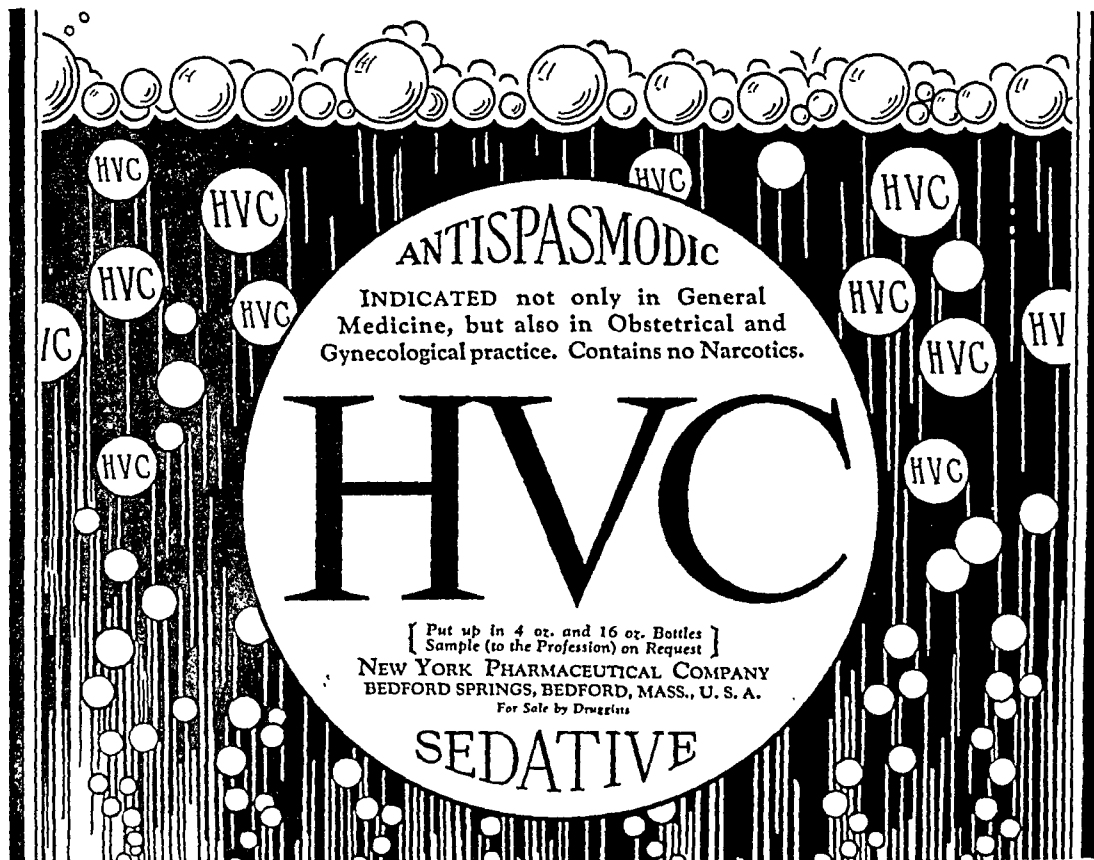
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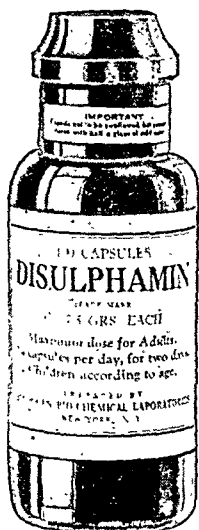
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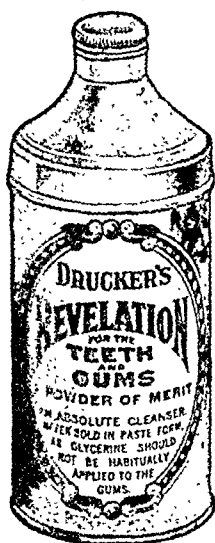
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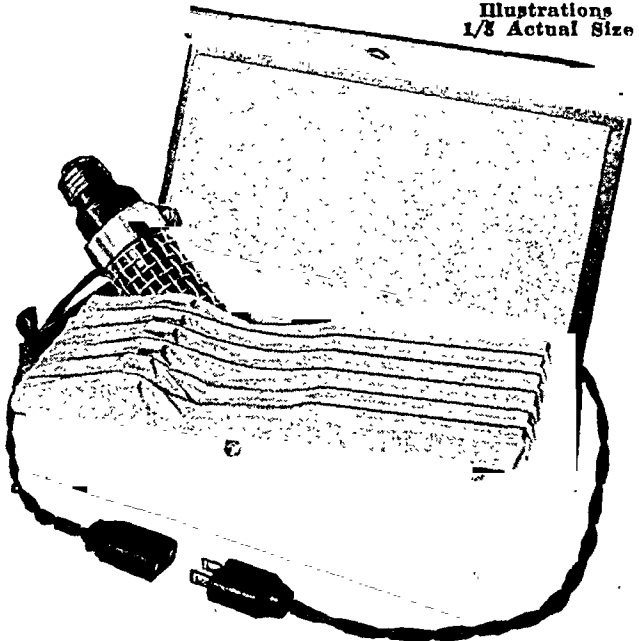
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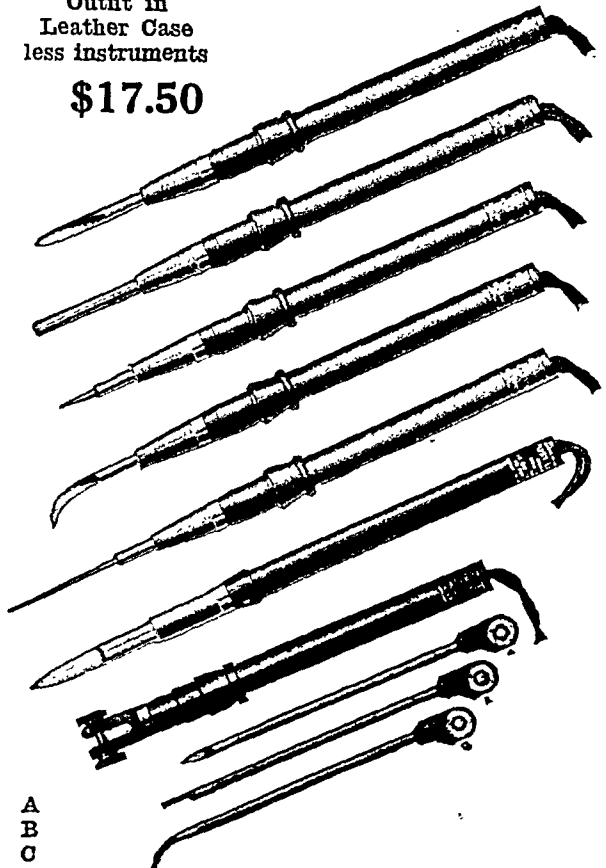


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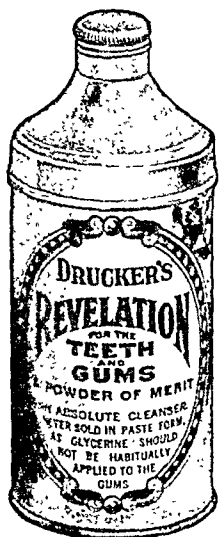
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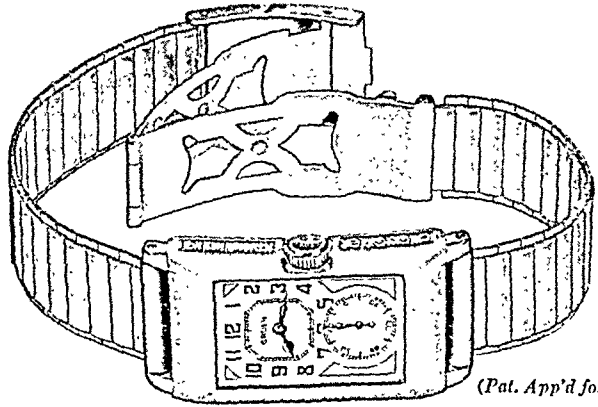
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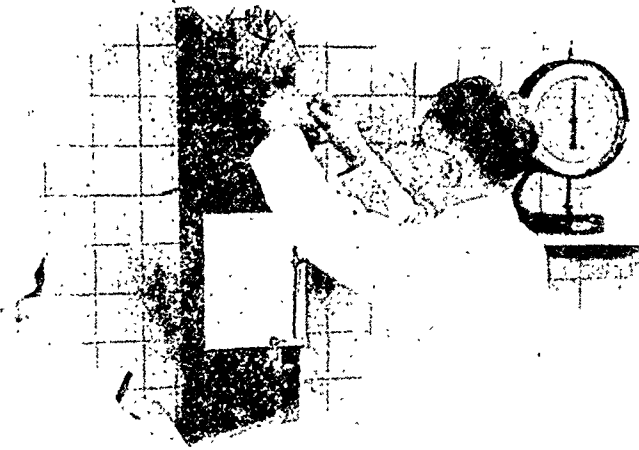
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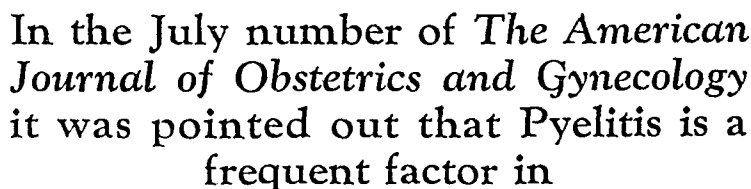
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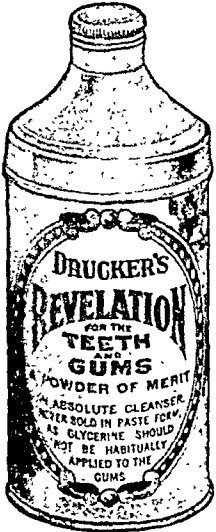
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No one in this enlightened age would think of feeding an individual on any single food exclusively, whether it be cereal or milk or fruit or vegetable, and surely not on butter or salt or sugar alone. Why, then, conjure up the specter of sugar as if it were an unmodified menace



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Our essential foodstuffs, when pure, would soon pall on the palate and by monotony lead to satiety and disgust. Particularly at the present time, there is a growing need of condimental foods—of improved flavor in our modern dietary regimen. The value of sugar as a condimental food, a physiological flavor, has never been more clearly indicated. A dash of sugar on our cereal, our fresh fruit, in our vegetables as they are being cooked, on our dish of bran, or even in the adolescent's indispensable glass of milk, may help to overcome an anorexia, and thus lead indirectly to a better regimen. Good food promotes good health.

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# Hypersensitiveness During Pregnancy

Frequently, during pregnancy, the gums become inflamed, sore and very sensitive.

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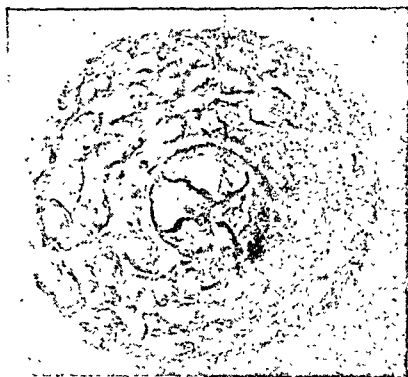
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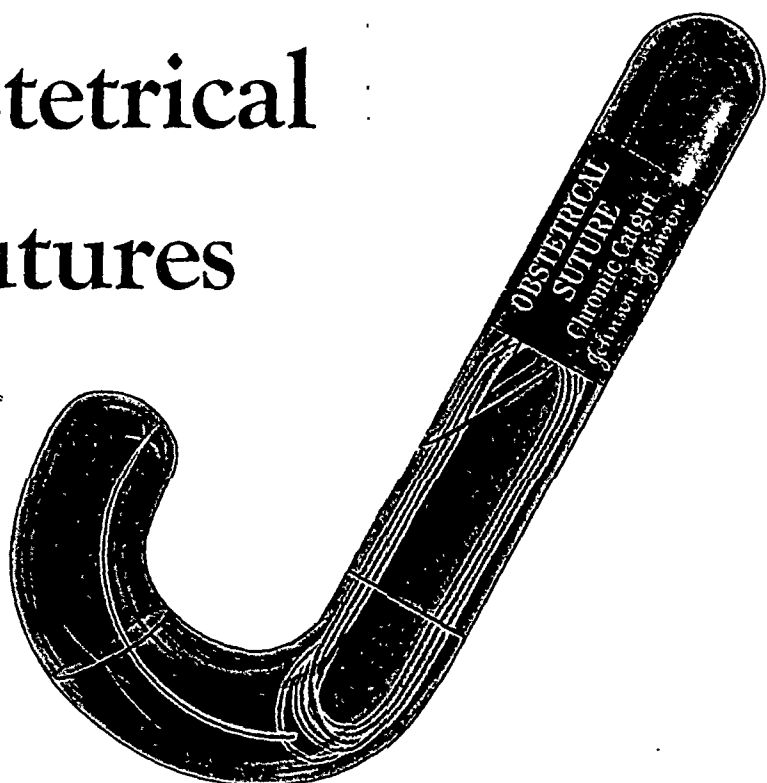
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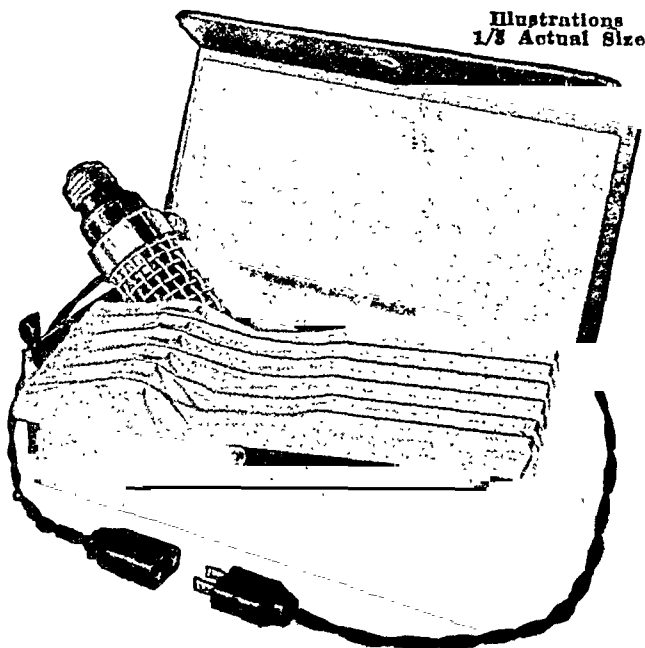
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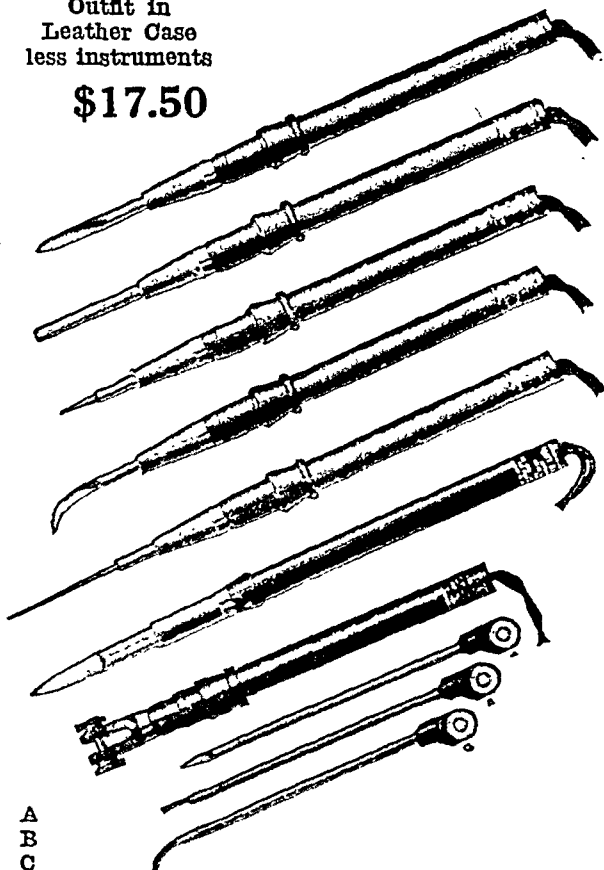


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The use of this solution should be continued as an antiseptic after the breasts heal and the infant is nursing again.

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# The American Journal of Obstetrics and Gynecology

VOL. XVIII

ST. LOUIS, AUGUST, 1929

No. 2

## Original Communications

### SPINAL ANESTHESIA IN OBSTETRICS AND GYNECOLOGY\*

BY GEORGE P. PITKIN, M.D., TEANECK, N. J.

IT IS said that all medical and surgical procedures must go through three stages of development. First, the optimistic stage, second, the pessimistic period, and third, the time of adjustment. This appears to be true of spinal anesthesia, perhaps more so than some of our other procedures. The stage of optimism may be easily accounted for, with the American people in particular, as they are always ready and grasping for something new, something spectacular. This overenthusiasm influenced many surgeons to take up spinal anesthesia without first familiarizing themselves with the technic. They often would not take the time or trouble to gain, even, a fair knowledge of the physiologic actions of the drugs.

In the early days of spinal anesthesia, one had to contend with more toxic drugs, it is true, than are now available but much of the pessimism was due, to a great extent, to the bad results reported by men who knew little or nothing about the procedure and would not take the time to familiarize themselves with its intricate value. The time of readjustment, if such has arrived, has been brought about by the earnest endeavor and research of those men who really strived to solve its mysteries.

Ephedrine, has possibly, contributed as much to the safety of spinal anesthesia as did adrenalin to the success of local anesthesia. The regulation of the specific gravity of the solution injected, either light or heavy, is almost as old as the method itself, as well as the attempts at producing viscous solutions with various tenacious substances, such as acacia, gum arabic, etc., in an endeavor to control the anesthetic solution in the dural sac. Amyloprolamin, a refined soluble gliadin.

\*Read at a meeting of the Philadelphia Obstetrical Society, December 6, 1928.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."



extracted from the mucilaginous content of wheat starch, produces a viscid solution that will prevent diffusion of the anesthetic solution with the spinal fluid until such time as the anesthetic agent has become fixed or absorbed. It reduces the toxicity of the anesthetic drug and places it under the control of the operator, permitting him to anesthetize as few or, as many groups of spinal nerves as is considered necessary to produce anesthesia of the desired field.

By limiting the contact of the solution to only those strands of the cauda equina, that form the sacral nerves, we were able to produce intradurally, sacral anesthesia in over 99 per cent of our cases, within three minutes. This form of anesthesia anesthetizes the cervix, vagina, vulva, perineum, and anal sphincter. The limited contact of the anesthetic to the extreme tip of the dura, causes no anesthesia of the hypogastric plexus, therefore normal uterine contractions are not inhibited. The result is, a painless childbirth.

#### INDICATIONS

I do not desire to advocate this form of anesthesia as the best or as one of choice, but we are often confronted with complications of pregnancy, where any form of inhalation anesthesia is absolutely contraindicated, therefore, it would seem worth while, at least to have a working knowledge of controllable spinal anesthesia to compete with certain complications. Tuberculosis, either arrested, chronic, or active, is often associated with various lung complications after inhalation anesthesia and the dormant, or arrested cases, are often converted into active lesions.

A woman suffering with acute or chronic bronchitis, should not be subjected to the possibility of a fatal pneumonia by giving her any form of inhalation anesthesia.

Patients suffering with asthma or emphysema are offered almost instant relief with controllable spinal anesthesia. This may be due, in part, to the ephedrin. Asthmatics cannot tolerate inhalation anesthesia.

Cardiacs with broken compensation are relieved at once. The cyanosis that accompanies each labor pain is relieved, and the patient is able to breathe with ease and if apnea is present, they are able to resume a reclining position comfortably within three or four minutes.

The toxemias of pregnancy are not affected by its use. There is no suppression. Elimination is not affected and dehydration is not produced by vomiting or aggravated by withholding of fluids.

Acidosis, which invariably accompanies the toxemias, is frequently relieved or greatly lessened. It is never increased. Acetone and diacetic acid disappears from the urine rapidly. The carbon dioxide content of the blood is not altered.

Nephritics, without eclamptic symptoms, are not subjected to the hazards of inhalation anesthesia.

Diabetics, a severe complication at best, has been shown by Joslin to respond better to spinal than any other form of anesthesia.

It has less effect on patients suffering with exophthalmic goiter or toxic adenoma, than does inhalation anesthesia.

The anemias of pregnancy are not affected by its use, as there is less hemorrhage at the time of delivery, no dehydration, or change in the blood chemistry.

Shock, caused by prolonged or tedious labors, may be carried through successfully with the free, but judicious use of ephedrin. The degree of shock is never increased after the administration of the anesthetic and oftentimes, improves materially.

The rigid spasmodic or cartilaginous cervix may be quickly and easily dilated manually. Light inhalation anesthesia, has little or no effect on this condition.

The extreme relaxation of the soft parts, even in a primipara, permits of the application of forceps with greater ease and the extraction of the child with less effort. The cooperation of the conscious mother and the normal uterine contractions, assist materially in the delivery. There is less trauma to the child and fewer lacerations.

In breech presentations the fate of the child is better, broken arms and legs are less frequent and delivery is performed with less effort.

In a case of prolonged labor, with the measurements of the mother and fetal parts normal, a rest period may be offered by mechanically expanding the solution from 4 to 6 c.c. This will cause uterine contractions to cease for two to three hours, when the pains are resumed, the mother is rested and able to help to a greater advantage.

Bandl's ring does not respond to inhalation anesthesia, unless carried to a dangerous stage and then, only with ether. Nitrous oxide or ethylene will have little or no effect in relieving the spasmodic condition. Spinal anesthesia if carried higher in the canal will relieve the contraction at once.

When versions are contemplated, the anesthetic should be expanded to 6 c.c., by mixing with spinal fluid, as this will abolish the tetanic contractions. There is no shock to the mother during the manipulations. She will laugh with you, as she has no discomfort.

Pituitrin may be used without harm, if given after the anesthetic, providing of course, obstetric judgment is used. It would seem to have some advantages over sacral or caudal anesthesia due to its quicker action, three minutes, as well as its certainty. There is no fifteen to twenty minute delay or 25 per cent of failures.

It has advantages over ordinary spinal anesthesia, in that, it does not affect normal uterine contractions, unless so desired by the operator. There is no vascular relaxation, nausea, vomiting, pallor, or cold sweats. Opiates are not necessary, such as morphine and scopolamine.

Its advantage over inhalation anesthesia is that there is no effect

on the heart, lungs, kidneys, or other vital organs of the mother. Post-operative lung, intestinal or kidney complications are nil.

When narcotics are employed or any form of inhalation anesthesia is administered to a pregnant woman at term, unquestionably some of the toxins of the agents are absorbed by the child, producing cyanosis and oftentimes rendering resuscitation difficult. This form of anesthesia in no way affects the well-being of the child.

#### ADVANTAGES

It assures the cooperation of the mother throughout delivery. She is able to change her position if desired, to bear down and aid in delivery without painful sensations.

It may be given to patients suffering with any of the complications of pregnancy without aggravating the condition.

Hypertension is not affected. Hypotension may be regulated by the use of ephedrin or by ephedrin and epinephrin combined. Our lowest case had a reading of 74/40, at the end of delivery, 120/68.

The absence of dehydration and suppression is a distinct advantage in toxemias and eclamptics.

There is no shock or postpartum reaction. Severe or prolonged cases are carried through with little or no change.

It increases the patient's comfort during and after delivery.

Vomiting during and after delivery is a rare occurrence.

Postpartum hemorrhages are less frequent. The uterus contracts firmly and quickly when it is emptied.

The cervix and perineum are protected to a greater extent from trauma and lacerations. The amount of relaxation and elasticity of these parts when anesthetized is amazing. Cystoceles are less apt to be a postpartum complication because the sphincters of the bladder are anesthetized and it, therefore, spontaneously empties itself.

Vaginal cesarean section may be obviated, as the cervix readily dilates, or it may be dilated manually with ease.

The mortality and morbidity of obstetric cases are reduced, because shock to the mother or postpartum anesthetic complications do not occur. The child is offered greater protection, because there is less trauma in forcible deliveries as a result of the relaxation of the soft parts, and because there is no absorption of toxins from narcotics or inhalation anesthetics.

Last but not least the obstetrician may be his own anesthetist, a distinct advantage in isolated practices, small hospitals without interns, or emergency night work.

#### TECHNIC

When local, conduction or spinal anesthesia is used, the paramount issue at all times is never to hurt the patient in any way at any time. A patient once hurt may lose confidence in the method and in the doc-

tor. A confidence once lost may be very hard to regain and many times constitutes the direct cause of unsuccessful anesthetics. A patient who is immediately subjected to one painful manipulation becomes overapprehensive of every following procedure. In spinal anesthesia with novocaine, tactile sensation is not abolished. All the more reason why every precaution should be taken and the technic employed with such finesse, that spinal anesthesia may be administered without producing any pain. With an entirely satisfactory anesthesia, the patient should be at ease, comfortable, and cheerful throughout delivery.

To perform the lumbar puncture, raise the head of the delivery table from 15 to 20 degrees. This degree of elevation is hard to judge but is readily measured by the use of the tiltometer. The patient is then in a slightly reverse Trendelenburg position and should be kept so throughout the course of delivery. If for any reason this is impossible she may be placed nearly flat, but not until after the anesthesia has become fixed, namely from twelve to fifteen minutes. If an adjustable delivery table is not available, pillows may be employed to secure a similar position.

The patient should be turned on her side, preferably the right. The knees should be flexed upon the abdomen, the head bent forward, so that the chin rests on the chest, and the back bowed out. The shoulders and hips should be in a vertical line. If the shoulders are tilted and the hips remain vertical or if the hips are tilted and the shoulders perpendicular, a corkscrew spine will be produced and may present difficulty at the time of puncture. A scaphoid back should be avoided as this causes the spinous processes of the vertebrae to override and makes puncture difficult and painful. If the physician is unfamiliar with the technic of this position, the patient may be permitted to sit on the edge of the delivery table with the feet hanging over the side, the body bent forward, the elbows resting on the knees and the back bowed outward. She may be permitted to remain in this position for from ten to twelve minutes until anesthesia becomes fixed or may immediately be placed in a semireclining position with the head of the table elevated as already described. However in the sitting position the patient's comfort and ease is disturbed. Never permit the patient to lie entirely flat or in a Trendelenburg position (22 degrees) when the heavy solution is used, as there is danger that the solution may ascend high in the canal and produce a drop in blood pressure, nausea, vomiting, and headaches.

The skin from the eighth dorsal to the lower part of the sacrum is painted over an area 5 or 6 inches wide with a 3 per cent tincture of iodine. If for any reason iodine is contraindicated, 5 per cent mercurochrome may be substituted. The logical site to introduce the spinal puncture needle for this particular form of anesthesia would be the lumbosacral interspace so as to introduce the anesthetic solution directly at the site of contact, but unfortunately in a number of cases we have found that the dural sac terminates above this interspace, therefore the fourth interspace is selected as the site of puncture. This may easily be determined by palpating the spinous processes along an imaginary line drawn between the crests of the ilia. When the interspace between the fourth and fifth lumbar vertebrae has been determined, it may be marked by firm pressure with the thumb nail of the gloved hand. At this site a cutaneous wheal is raised with 0.65 c.c. solution of novocaine, 0.013; ephedrine, 0.5; and normal saline q.s., 1.3.

A fine 25 or 27 gauge hypodermic needle is used. The needle is not withdrawn but is carried directly into the interspinous ligament and the other 0.65 c.c. of the solution injected as the needle advances. One should endeavor to inject the solution a little faster than the needle proceeds, so that the needle is introduced into

a freshly anesthetized area. To avoid the unpleasantness of having to dig out a broken needle it is advisable to have the needle equipped with a safety guard.

Spinal puncture is made through the center of the wheal, raised with the novocaine ephedrine solution with a fine 22 gauge lumbar puncture needle. The needle should have a short bevel of 45 degrees. The rear part of the bevel is rounded in such a manner that it has no cutting surface, while the reverse side of the point is ground so as to produce a spear point. When this needle pierces the dura it cuts a miniature trapdoor which is closed by the intradural pressure when the needle is withdrawn. The spear point of the tip permits easy penetration of the skin and tissues. For many reasons, rustless steel needles are superior to nickeloid or nickel-plated ones. In every case, the stylet should be removed and the needle bent into a semicircle before it is sterilized. This testing may prevent the unpleasantness of removing a broken needle from the interspinal ligament.

Avoid using a needle of large caliber, such as the old Bier 15 to 17 gauge needle, which will not only cause unnecessary pain, but will traumatize the tissues and often produce postanesthetic backache. A large needle may produce intradural hemorrhage or it may injure or cut the cauda and permit seepage of spinal fluid into the extradural tissues, because of the large hole left in the dura. Long, tapered needles produce bleeding more frequently at the time of puncture. With their use anesthesia is frequently unsatisfactory, because a part of the taper is within the dura and the remainder outside, or a part of the taper is within a vein and the remainder in the dural sac. Should only a part of the taper be within the dura, some of the solution is deposited extradurally. Anesthesia will be unsatisfactory or incomplete. Should part of the taper be within a vein when the solution is injected, convulsions may ensue. With a short tapered needle, these undesirable complications rarely occur. When the puncture is made through the interspinous ligament, care should be taken not to deviate to the right or left. The puncture should be at right angles to the long axis of the spine. Never attempt a puncture between the laminae. Avoid inserting the needle in an upward direction or at an acute angle to the spine. The veins about the cord are large and numerous but may be avoided and not penetrated if the spinal puncture is made in the manner described. Unnecessary bleeding will surely be produced should the puncture be attempted between the laminae with the needle tilted, with a needle of large caliber, or with a long tapered point.

When the dura is punctured there is a slight snap, which is recognized after the first few punctures, and the needle advances with less resistance. If possible, avoid piercing the opposite side of the dura with the point of the needle, or coming in contact with the body of the vertebra, because this also will cause bleeding. With the assurance that the dura has been entered, the stylet is removed and spinal fluid should flow through the needle. If no spinal fluid appears, rotate the needle on its own axis. If there is still no spinal fluid, insert the needle deeper. If bony resistance is felt (the body of the vertebra), the needle has undoubtedly deviated to one side. It should be withdrawn to the skin surface and reinserted at a slightly different angle to the right or left as the case may be. Always have the stylet in place when making manipulations. Occasionally the first drop or two of spinal fluid will contain blood. If this clears the injection may be made. If not, the needle should be withdrawn and reintroduced. The injection of the anesthetic solution should never be made until clear spinal fluid flows through the needle, which is the only assurance that the point of the needle is within the dural sac. Unless the solution is injected into the subarachnoid space, anesthesia will not be satisfactory.

It is advisable to fill both hypodermic syringes with the respective solutions before the spinal puncture is started. The filled syringes and needles should be placed in a convenient position to the operator before the procedure is started.

Attach to the spinal puncture needle the syringe with the solution containing: novocaine, 0.2; gliadin solution, 0.13; strychnine sulphate, 0.0022; glucose, 0.065; and normal saline, q.s., 0.5. Aspirate one or two drops of spinal fluid to make sure that the needle has not been displaced, then slowly inject the contents of the syringe. Do not again aspirate or in any way attempt to mix the solution with the spinal fluid. Withdraw the needle and cover the puncture wound with collodion or a small square of adhesive plaster. Turn the patient on her back. Anesthesia will be complete as soon as the patient can be prepared and draped. This procedure limits the contact of the solution to the lower tip of the dural sac and causes anesthesia of the perineum only.

It is better to have a syringe with a secure locking device to insure a tight fit to the needle, thus preventing the possibility of injecting air into the dural sac or leakage at the connection. With a locking device on the syringe, the needle may be manipulated, if necessary, and if the patient moves there is little chance that the syringe will be disconnected from the needle, and some of the anesthetic solution lost. With the locking device employed, needles never become "jammed" and there is no leaking at the connection.

The semireclining or reverse Trendelenburg position of from 15 to 20 degrees should be maintained for one and one-half to two hours after injection so as to avoid the possibility of having the anesthetic ascend in the canal; also by retaining the anesthetic low in the dural sac, headaches will be greatly diminished. If for any reason anesthesia is desired higher on the body surface it can be obtained by mixing the solution with spinal fluid. This is done by aspirating and reinjecting 2, 4, or 6 c.c. of the spinal fluid. Four c.c., aspirated and reinjected, will produce anesthesia of the legs. Six c.c. will carry anesthesia to the umbilicus and 8 c.c. to the costal margin. For the higher anesthesia the viscid alcohol solution is preferable as this will permit the patient to be placed in a level or Trendelenburg position. The heavy solution should never be used when the head is to be lowered.

Preoperative narcotics are not necessary in this form of anesthesia. The relief of pain afforded the mother, allays all fear and apprehension. Morphine and scopolamine, if used, may possibly so affect the child that strenuous resuscitation methods will be necessary. The mother may remain in a dorsal recumbent position or may be placed in stirrups without affecting the limitation of the anesthesia provided the body is kept in a reverse Trendelenburg of from 15 to 20 degrees.

It is hoped that my intentions will not be misconstrued. I do not wish to imply that this is the ideal or only form of anesthesia to be employed in obstetrics. It is offered as being, simpler, quicker and more efficient than caudal and as a method of relieving pain, suffering, and misery in those unfortunate cases in which any form of inhalation anesthesia would be detrimental or fatal to the mother, child, or both.

*(For discussion, see page 280.)*

# THREE PHASES OF GYNECOLOGIC PLASTIC SURGERY\*

BY ROBERT T. FRANK, A.M., M.D., F.A.C.S., NEW YORK

I HAVE chosen an extremely practical topic, namely, that of gynecologic plastic operations, a topic which has always interested me greatly, and a phase of our specialty which I feel is still to be clarified and technically improved.

As I propose to cover three main subjects, it will be necessary to be most summaristic and brief.

The three headings of my paper are: (I) principles underlying the repair of vesicovaginal fistula, (II) the treatment of prolapse of the uterus, rectocele and cystocele, (III) the construction of an artificial vagina by means of tube flaps.

TABLE I. PLASTIC OPERATIONS, 1925 TO 1928

	1925	1926	1927	1928	TOTAL
Plastic and ventrofixation	10	24	16	27	77
Plastic and ventrosuspension	3			3	6
Plastic, anterior and posterior	5	20	21	16	62
Plastic, anterior colporrhaphy	2	9	6	5	22
Plastic, posterior colporrhaphy	2	3	12	3	20
Ventrofixation		2	2	5	9
Le Fort operation		1	4		5
Interposition operation			2		2
Moschcowitz operation, rectal		3	1	1	5
Vesicovaginal fistula		2	4	3	9
Artificial vagina		1	2		3
Total					220

The table shows my material from the fall of 1925 to December, 1928. My remarks are, however, based upon an experience of twenty-five years and include a correspondingly larger number of cases.

## (I) REPAIR OF VESICOVAGINAL FISTULA

My personal experience is limited to 33 cases, due, in the main, to two causes, the one to obstetric, the other to operative injuries. The resulting defects varied from pinpoint in size to complete loss of the lower wall of the bladder, including the sphincter and urethra. It follows that no final conclusions can be drawn from statistics based on such a small number of cases, although at the present time, few individual operators have the opportunity of dealing with a large series.

*Old Technics.*—Of the older, well-established and useful technics, the freshening of the edges and direct suture by the Marion Sims method is still applicable in a considerable number of cases. If approximation without tension can be obtained either by liberating incisions at the

\*Read at a meeting of the Chicago Gynecological Society, December 13, 1928.

time of operation, or by preliminary dilatation treatments, the Sims technic is particularly useful in small or medium-sized defects in the region of the sphincter vesicae.

The flap splitting operation is of great value in a number of cases where the septum separating the bladder and vagina is of sufficient thickness to permit of separation of the two mucosae, and of separate suture of the bladder and vaginal mucous membrane. Where the septum is too thin, flap splitting is impossible.

*Newer Technics.*—Transposition of the uterus: In one instance I was able to close a large gap in the inferior surface of the bladder as well as to reestablish continence, by utilizing the superior surface of the transposed uterus to close the gap, as well as to supply pressure at the vesicourethral junction, and thus reinforce sphincter action. This method will be rarely utilizable.

Mobilization with or without suture: In 1917 I called attention to the technic which before and since then has stood me in good stead in cases of great technical difficulty, especially where the large size, and the presence of dense scars made the ordinary technics inapplicable.<sup>1</sup>

Sometimes by the vaginal approach, more often through the abdomen from above, and then preceded as a rule by a supravaginal hysterectomy for technical reasons, the bladder is widely mobilized. This mobilization must be done boldly and to such an extent that the entire defect is freed from the subadjacent tissues. If feasible, suture of the gap should be attempted. If not feasible, this has happened twice to me, the abdominal field is carefully extraperitonealized by union of the vesical and retrocervical peritoneum, and by securing a loop of the sigmoid over this first suture line. At the lower angle of the wound a rubber tissue drain may be placed down to the bottom of the space of Retzius. Under these conditions, the main and essential requisite for healing is a constantly functioning indwelling catheter by means of which the bladder is kept in a complete state of contraction for fourteen days. It will then be found that, just as sometimes happens in a spontaneously formed fistula arising postpartum, when similarly treated, complete healing of the bladder has taken place.

The reestablishment of continence: In mild cases, freshening and suture of the canal by the Sims technic closes the urethrovesical defect. It is then of the utmost importance to gather the fasciae, especially the triangular ligament, across the vesicourethral junction. This usually reestablishes complete control.

Reconstruction of a torn urethra is followed in a disappointingly frequent number of cases by dribbling of urine. No great effort need be wasted in establishing the full length of the urethral canal. Very short urethral canals, if the sphincter apparatus is intact, function perfectly.

I have had no gratifying results with elaborate neoformations of ure-



thrae. The canal has been satisfactory from a cosmetic point of view but functionally incompetent. Possibly subsequent use of the Stoeckel-Goebel technic might offer better functional effect. In one instance, I was able to construct and apply a pessary which exerted pressure against the new urethra, and thus gave a fair degree of continence.

At present I am more concerned with constructing a good vesical opening of small size (just admitting a No. 7 to No. 8 French catheter), the resultant closure being effective except on severe pressure and coughing.

## (II) THE TREATMENT OF PROLAPSE OF THE UTERUS, RECTOCELE AND CYSTOCELE

I have no intention of attempting to cover the entire subject, nor do I propose to weary you with an accumulation of statistics. On the contrary, I shall attempt merely to give you my own preferences which I have arrived at after prolonged and soul-searching efforts to find a generally applicable cure. I may say that every case is an individual problem and that depending upon the type of our material, the individual patient, and our own experiences and preferences, different operators have come to prefer different methods. I do not hesitate to assert that even in the best of hands, a minimum of 10 per cent of recurrences is bound to occur in a large material properly followed up.

(1) The interposition operation, which was so largely worked out in Chicago, is but rarely used by me and is then employed in women past the menopause, with a small but not too small uterus, suffering from what I designate as a billiard ball cystocele, complicated by not more than a first degree of prolapse.

(2) Vaginal hysterectomy: I have used this operation twice in cases of prolapsed uteri in which adenocarcinoma simultaneously necessitated removal of the uterus. Today, if such a case should again confront me, I would prefer the abdominal route with fixation of the vaginal stump in the abdominal fascia. I have seen no more desolate condition than recurrence of prolapse in cases in which the uterus was removed for its cure and in which a subsequent eventration of the pelvic floor resulted. Under these conditions nothing but complete excision and obliteration of the vagina is possible.

The Le Fort operation of producing a median longitudinal septum has proved unsatisfactory in the few cases in which I employed this technic.

(3) *Anterior and Posterior Colporrhaphy With Ventrofixation.*—In all cases of complete prolapse, in all large rectoceles and cystoceles, if operation is undertaken (and this will exclude women in the child-bearing period who still desire further progeny) I am in the habit of performing an anterior and posterior colporrhaphy according to the technic which I have described, in 1917<sup>2</sup> and 1922,<sup>3</sup> followed at once,

or at a later date, as I shall explain, by extraperitoneal ventrofixation of the uterus.

(4) This operation is unsuitable in women who still desire to have children. In selected cases, an anterior and posterior colporrhaphy, and a careful Alexander-Adams shortening of the round ligaments have been used in young women who have thereupon successfully borne children without recurrence of their prolapse, although a certain number may be expected to recur with or without subsequent childbirth.

(5) In every case where abnormal bleeding has been noted, a curettage is performed at the time of the plastic operation. Curettings suspicious of malignancy, or the possibility of early pregnancy, as sometimes happens, demand postponement of the plastic operation until microscopic confirmation of the findings has been obtained. In the case of early pregnancy and abortion, the main operation should be postponed for at least four months.

(6) Amputation of the cervix has been performed less and less often as a preliminary step. By confining the patient to bed for one or two weeks before operation, ulcerations are healed, and hyperplastic, edematous cervixes show a gratifying involution.

*Anesthesia.*—Particularly in my ward hospital practice, many of the candidates for plastic operation are found to be short, overweight, afflicted with high blood pressure, with poor myocardiums, often impaired renal function, emphysema, and bronchitis, in other words, far from attractive or safe operative risks. Such patients formerly were strong arguments in favor of selecting a short method, such as the interposition operation by means of which the cystocele as well as, in certain cases, prolapse of the uterus is overcome.

Today, however, I use parasacral anesthesia in these patients, obtaining a surprisingly relaxed and painless field, postponing the ventrofixation until the vaginal plastic has entirely healed, usually a matter of from fifteen to eighteen days. The ventrofixation is then performed rapidly under gas oxygen anesthesia with very little postoperative reaction.

I need hardly say that to the ventrofixation performed during the childbearing period, ligation of the tubes is always added.

*Technic.*—The actual technic requires little elaboration.

The anterior colporrhaphy is performed by fully exposing the pubocervical fascia which is not only brought together but is also transplanted to a higher level on the cervix after the bladder has been thoroughly liberated, thus effectually holding back that viscous.

The posterior colporrhaphy is performed by means of a simple Hegar triangle or a linear longitudinal incision. The rectum, in cases of high vaginal enterocele, is fully freed from the herniated Douglas sac. The peritoneum is resected, as in any hernia, and a suture brings together the anterior surface of the rectum, the two sacrouterine ligaments and

the posterior surface of the cervix, thus closing up the Douglas defect. Thereupon a perineorrhaphy is superadded by bringing together these fascial planes which cover the rectum (fascia recti), as well as those which cover the levator muscles. I have found exposure and suture of the levator ani muscle leading to thin, scarry, painful perineums.

Ventrofixation through a small incision is performed by means of a slightly modified Kocher technic in which the fundus of the uterus is extraperitonealized by means of a peritoneal suture, the uterine tissues being brought in direct contact with the fascia of the external oblique and sutured there with chromic catgut.

Tying of the tubes, when necessary, is performed by passing a thin silk suture (the only occasion in which I use silk in surgery) through the mesosalpinx at the beginning of the ampullary end of the tube, forming a sharp angle loop of tube, and tying this same suture across each piece of the loop. Care should be taken not to tie the suture so tightly as to favor cutting through. The top of the tubal loop is then snipped off, leaving a double barreled lumen which, in my experience, has shown no tendency to reformation of continuity.

Special technics: In five instances in the presence of large fibroids, I have found it necessary to perform a supravaginal hysterectomy for the tumor where large rectocele and cystocele as well as weak cardinal ligaments made the subsequent occurrence of inversion of the vagina certain.

In these cases, I have performed a supravaginal hysterectomy leaving a long cervical stump.

The cored out cervical stump was carefully sutured. Before further repair was then undertaken, the bladder was pushed away from the vagina, in the median line, down to the urethrovesicle junction, and thereupon the typical Polk operation was performed. This, as you will see, consists in bringing the pubocervical fascia together below the bladder, just as I do by the vaginal route, only using the abdominal approach. Great care must be exercised in keeping close to the median line, otherwise serious hemorrhage may result. After closure of the fascial planes, the vesicle peritoneum is sutured to the anterior surface of the stump which, however, as in the early operation for abdominal hysterectomy, is left extraperitoneal and is fastened to the fascia of the external oblique just as the fundus of the uterus is fastened in the ventrofixation technic previously described.

In 5 cases the operation has proved satisfactory. When necessary, and this usually is so, a posterior colporrhaphy is performed at a later session.

The reason for selecting the Polk operation in these cases is that if the anterior colporrhaphy is performed after ventrofixation of the stump, it is quite likely that the stump will be torn from its abdominal

anchorage during the manipulations necessary in exposition of the anterior vaginal wall.

### (III) CONSTRUCTION OF AN ARTIFICIAL VAGINA

The danger of the Baldwin operation in which only partial statistics show a mortality of 20 per cent, the sloughing and stenosis following the Schubert rectal technic, have prevented me from ever attempting these operations for the reconstruction of an artificial vagina.

Dr. Samuel Geist and myself have devised a method based on the tube flap technic which we learned during our war experience, and which has served us in an encouraging fashion in the two cases completed and the one case in process of construction.<sup>4</sup> I limit this operation to feminine individuals in whom I have been able to demonstrate a cyclical accumulation of female sex hormone in the blood, whose psychic inclination toward the male is well marked, and in whom weighty personal and social factors incline me to follow their wishes. The two first patients were married and threatened with divorce. Two young women at present under treatment are engaged to be married. Another one who will be started within the next few weeks is engaged and her fiancé is fully aware of her disability. A fourth patient is obliged to submit to the operation because of the unhappiness resulting from family disagreement, as her parents insist that she qualify for the marriage state.

The operation, we have found, is free of risk, requires at the minimum eight weeks of more or less intermittent hospitalization, but offers a very excellent chance of the permanent establishment of a satisfactory vagina. In one case in which I attempted to shorten the steps by using a direct flap instead of the tube technic, complete necrosis of these skin flaps resulted.

We feel confident that the tubulization gives a tremendous additional vitality and independence to the flap and enables us to utilize it with a great degree of impunity.

The steps consist in brief (1) in the formation of one or more bilateral tube flaps which are well described as "satchel handle flaps." After full healing has taken place (2) an incision is made between rectum and urethra, closer to the rectum, in order to obtain as large and movable an anterior flap of vestibular mucosa as is possible, and by means of blunt dissection, a false passage is established in the *rectourethral septum* until the peritoneum is reached. (3) The distal portion of the tube flap is severed, (4) the tube is reopened throughout its pedicle, fully mobilized, and (5) the skin is spread over a vaginal plug with the skin surface toward the plug. (6) By means of this prothesis, the flap is introduced and fixed in the false passage. (7) The free distal end of the flap is sutured to the raw skin edge of the vagina. (8) A permanent catheter is introduced into the urethra. (9) After

ten to twelve days, depending on the type of healing, the pedicle at the vulvar margin is severed, the stump of pedicle used to cover any defect on the thigh, the free end of the flap being sutured to the freshened vulvar margin. (10) A vaginal plug is worn constantly for the first two months and thereafter for another eight to ten months during the night.

These are the technics which have stood me in good stead. They still can be improved upon in principle as well as in details of execution. The operations require minute care, some operative experience and manipulative skill. They possess the advantage of being anatomic and therefore can be readily taught. The results are permanent and satisfactory.

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10 EAST EIGHTY-FIFTH STREET.

(For discussion, see page 287.)

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**Rühl, A.**: Noktol as a Soporific in Child-bed, München. med. Wehnschr. 73: 863, 1926.

Noktol, whose chemical formula is isopropyl-brompropheynl-barbituric acid, was tried in 30 cases, twelve normal deliveries, eight cesarean sections, and ten forceps deliveries, the dosage being two tablets of 0.1 gm. each; one tablet of 0.1 gm. was insufficient. This drug was very effective following operations, normal physical sleep occurring in one-half hour. There was no bad effect on mother or child. Neither bromide ion nor barbituric acid radical passed into the milk. Noktol is very safe in doses of 0.2 gm. following operation and in fever.

WILLIAM B. SERBIN.

**Hinselmann**: Leucorrhea, Ztschr. f. Geburtsh. u. Gynäk. 93: 349, 1928.

The author uses a telescope, magnifying up to 40 times with intense light, to examine the vaginal wall and finds that there are inflammatory changes visible in 60 to 70 per cent of all cases having leucorrhea. He believes that endocervicitis following gonorrhea is much less common than vaginitis. Leucorrhea coming from the endometrium is found only in from 10 to 20 per cent of cases. The discharge may be seen being expelled from the cervix if observation is continuous for up to twenty minutes. The differentiation of the source of a leucorrhea is made by this method of examination with the addition of the microscopic examination of small pieces of tissue excised from different parts of the genital tract which appear to be inflamed when looked at with this telescope.

FRANK A. PEMBERTON.

# THE OUTCOME OF 625 PREGNANCIES IN WOMEN SUBJECTED TO PELVIC RADIUM OR ROENTGEN IRRADIATION\*

By DOUGLAS P. MURPHY, M.D., PHILADELPHIA, PENNSYLVANIA

(From the Gyneccean Hospital Institute of Gynecologic Research, University of Pennsylvania)

THE present paper is a study of the outcome of 625 pregnancies occurring in women who were subjected to pelvic radium therapy or roentgen irradiation either before or after conception took place. The data were secured from a review of the literature,<sup>4</sup> and from the answers to a questionnaire sent to more than 1700 leading gynecologists and radiologists in this country.<sup>5</sup> The material under discussion concerns the influence of irradiation upon the duration of pregnancy, and its effect upon the health and development of the subsequent children. Wherever the term irradiation is employed, *therapeutic* irradiation is implied, unless otherwise stated. In every case the treatments were directed toward the pelvic region; in most instances they were instituted for diseases of the pelvic organs, although in one or two cases the pelvic irradiation was employed for the purpose of inducing sterility because of the existence of a systemic disease.

## THE INFLUENCE OF IRRADIATION UPON THE DURATION OF PREGNANCY

Approximately 24 per cent of the 625 pregnancies terminated in abortion (Figs. 1 and 2). The exact abortion rate for nonirradiated women is difficult to secure. DeLee, in a personal communication,<sup>1</sup> and as quoted in a previous paper,<sup>4</sup> presents figures that indicate that for certain continental cities in Europe the rate is approximately 33 per cent. If this figure can be accepted as a fair one for comparison, the rate of abortion among the irradiated women in this series would not seem to have increased as the result of the treatments.

When, however, the abortions among irradiated women are considered independently, and are grouped according to the time of treatment with respect to conception (Fig. 3), it is found that the rate is higher when irradiation was instituted after conception had taken place than when it preceded conception.

## INFLUENCE OF IRRADIATION UPON THE HEALTH OF THE CHILD

For the purpose of this study the term "unhealthy child" is applied to any child born at or close to term of a mother who has received pelvic radium treatment or roentgen irradiation either before or during pregnancy, the child presenting at any time any disturbance of

\*Read, by invitation, at a meeting of the New York Obstetrical Society, December 11, 1928.

health or defect of development, mental or physical, or who may have died while under observation, from whatever cause. This definition was made to include those children who showed even the mildest forms of ill health, in order that no deviation from the normal that could have resulted in any way from the previous maternal treatment might be overlooked. The scope of this definition has made it practically impossible to secure any satisfactory control statistics, with which those under discussion might be compared.

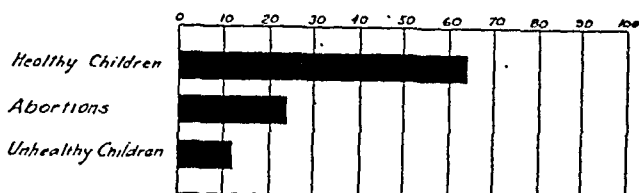


Fig. 1.—The outcome of pregnancies associated with pelvic irradiation. Showing the outcome of 625 pregnancies in women subjected to pre- or postconception pelvic radium or roentgen irradiation, with respect to the percentage frequency of subsequent healthy children, abortions, and unhealthy children.

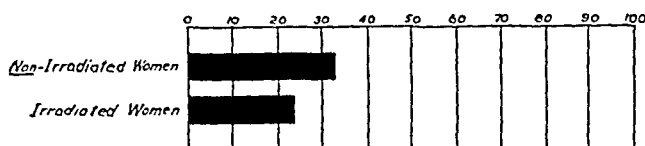


Fig. 2.—Abortion rate. Showing the abortion rate (expressed in percentage) as it occurred in 625 pregnancies associated with either pre- or postconception irradiation, as compared with the rate for nonirradiated women (DeLee). Note that the abortion rate was lower for the irradiated women.

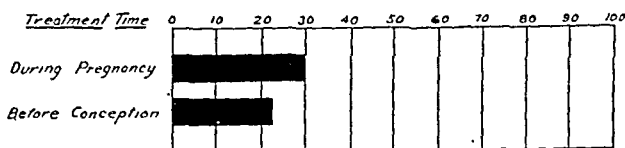


Fig. 3.—The effects of the treatment time upon the abortion rate. Showing the abortion rate (expressed in percentage) in 106 pregnancies in which the irradiation was postconception in time, contrasted with the rate for 519 pregnancies where the irradiation preceded conception. Note that the rate is higher when the treatment is postconception in time.

*The Frequency of Unhealthy Children.*—Sixty-five per cent of the 625 pregnancies studied terminated in the birth of healthy children (Fig. 1), whereas 12 per cent (76 children) were classified as unhealthy, according to the definition previously given. A morbidity of 12 per cent has little weight here, since it is impossible to estimate the morbidity rate for children born of women with pelvic and other serious disorders who have not been irradiated, with which to compare the present rate.

*Influence of the Time of Treatment Upon Child Health.*—Considering the unhealthy children alone, and grouping them according to the time that maternal treatment with respect to conception was administered,

we find (Fig. 4) that unhealthy children appeared more frequently following postconception irradiation than after preconception treatment of the mothers. This is one of the most important facts brought out by this study.

*Classification of Unhealthy Children.*—The pathologic disturbances observed in the 76 unhealthy children previously mentioned are, for convenience of study, divided into four groups (Fig. 5): (1) Children presenting gross structural deformities; (2) those born weak or diseased, but who were still living at the last observation; (3) children who were stillborn; and (4) those who died while under observation.

*Method of Presentation of the Data.*—The 76 unhealthy children are divided into two main groups: (1) Those children who were born after

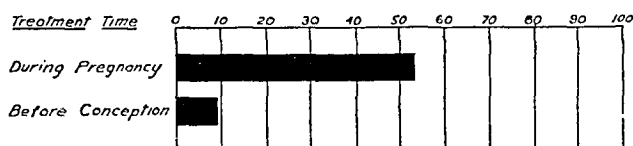


Fig. 4.—Child health with relation to treatment time. Showing the percentage of unhealthy children born of irradiated mothers, arranged according to whether the treatments were postconception or preconception in time. Note the high frequency of health disturbances appearing in the children born following postconception irradiation.

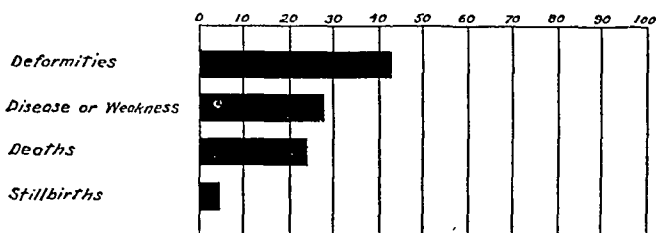


Fig. 5.—A classification of child health disturbances. Showing the relative frequency in percentage of the more important groups of child health disturbances appearing in 76 children born after preconception or postconception maternal pelvic irradiation. Note that gross deformities were the most common abnormality of child health.

preconception irradiation of the mother; and (2) those who were irradiated in utero or were born after postconception treatment. Each of these groups is discussed separately, the four subgroups as outlined in the preceding paragraph being taken up for consideration.

#### PRECONCEPTION IRRADIATION

In this group there are 38 children who were born following maternal preconception pelvic irradiation.

*Stillbirths.*—The stillbirth rate for women having received preconception irradiation was less than one in 100 of live and dead births (Table I). Statistics quoted by Falk<sup>3</sup> for the United States registration area for the year 1918 gave the rate as 3.5 per 100 of live and dead births. From this comparison it would seem that the stillbirth rate was not increased by reason of the previous maternal irradiation.



*Deaths.*—The death-rate of children under one year of age born of mothers having received preconception pelvic irradiation was not more than 32 per 1,000 of live births (Table II). In this group there was included one death after one year of age, i.e., a child who died of pneu-

TABLE I. PRECONCEPTION IRRADIATION

	NUMBER	PER CENT
<i>Stillbirths:</i>		
Full-term pregnancies	402	100.0
Stillbirths	4	0.9
Causes:	Two unknown.	
	One due to knotted cord.	
	One due to eclampsia.	

monia at eighteen months. According to the reports of the United States Bureau of the Census, the death rate for children under one year of age for the year 1927 was between 76 and 100 per 1000 of the population. A comparison of these two groups of figures would seem to indicate that maternal preconception irradiation did not cause any increase in the infant death-rate.

TABLE II. PRECONCEPTION IRRADIATION

	NUMBER	PER CENT
<i>Deaths:</i>		
Full-term pregnancies	402	100.0
Deaths	13	3.2
Causes:		
Respiratory	6	
Bronchitis (few days, 9 months)	2	
Pleurisy (11 months)	1	
Pneumonia (2 days, 11 months, and 18 months)	3	
Obstetric	5	
Eclampsia	3	
Prematurity	1	
Dystocia	1	
Unknown	2	

*Disease and Weakness (Without Death).*—As is shown in Table III, among the children born after preconception pelvic irradiation, a morbidity rate of less than 4 per cent was noted. No series of control figures could be secured with which these figures might satisfactorily be compared. The nature and variety of these disturbances, however, would lead to the conclusion that the irradiation played little if any part in their production.

*Gross Deformities.*—Few gross deformities were found among the children born following preconception ovarian irradiation (Table IV), and those that were found, although severe in some cases, varied

greatly in type. There seemed to be no uniformity that might suggest a common cause. These facts should be borne in mind when considering the gross deformities observed among the children born following postconception irradiation.

TABLE III. PRECONCEPTION IRRADIATION

	NUMBER	PER CENT
<i>Diseases and Weakness (Without Death):</i>		
Full-term pregnancies	402	100.0
Diseases or weakness	14	3.4
Underweight	4	
Rickets	3	
Difficult feeding	2	
Pulmonary tuberculosis	1	
Learns poorly	1	
Pale, walked at 17 months	1	
Anemic and thin	1	
Weak and frequently sick	1	

TABLE IV. PRECONCEPTION IRRADIATION

	NUMBER	PER CENT
<i>Gross Deformities:</i>		
Full-term pregnancies	402	100.0
Deformed children	7	1.7
Microcephaly	1	
Anencephaly	1	
Parietal bone defect	1	
Deformity, no description	1	
Congenital heart defect	1	
Tracheal stenosis	1	
No right forearm or thumb	1	

*Frequency of All Health Disturbances (Preconception Irradiation).—*Fig. 6 shows the relative frequency of health disturbances appearing in the 38 children born following preconception irradiation, as pre-

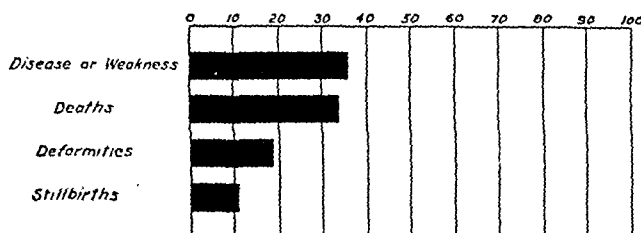


Fig. 6.—A classification of health disturbances in children born after maternal preconception pelvic irradiation. Showing the relative frequency, as expressed in percentages, of the classified health disturbances appearing in 38 children born following preconception pelvic irradiation.

viously classified. Although death and disease and weakness (without death) are somewhat more frequent than are stillbirths and deformities, there are no wide differences between any of them, as will be observed among the health disturbances noted in the children irradiated while in utero.

*Discussion.*—Among the health and developmental disturbances seen among the children born after maternal preconception irradiation, there are no outstanding and clear-cut indications that the irradiation alone was responsible for them. The small number of such disturbances, their lack of uniformity, and the fact that practically nothing is known concerning other etiologic factors and their influence on the irradiated women, would suggest that, in all probability, the irradiation was not an important agent in their production. Furthermore, little, if anything is known concerning the causes of similar deviations from the normal found among children born of women who have *never* received pelvic irradiation. Again we do not know to what extent, if any, physiologic disturbances of the pelvic organs in women exert a detrimental effect on the health of subsequent offspring. All these considerations tend to inject some doubt into the belief that the maternal irradiation may have injured the health of the children under discussion.

#### POSTCONCEPTION IRRADIATION

Among the children who were irradiated in utero, 38 were found to be unhealthy. The disturbances found to exist in these children may be grouped and analyzed as follows:

*Stillbirths.*—Table V shows that no stillbirths were observed in this group of children *irradiated in utero*. The entire group is quite small, perhaps too small to have any statistical value. It will, however, suggest, at least, that the irradiation of the child in utero did not increase the percentage of stillbirths.

TABLE V. POSTCONCEPTION IRRADIATION

	NUMBER	PER CENT
<i>Stillbirths:</i>		
Full-term pregnancies	74	100.0
Stillbirths	0	0.0

*Deaths.*—The death rate for the full-term children under one year of age irradiated while in utero is shown in Table VI. This is approximately 54 per 1000 of births. Statistics for the registration area of the United States for the year 1924 reveal an infant death rate of 76 per 1000 births. A comparison of these figures would tend to show that the maternal irradiation postconception in time, had no influence upon the infant death rate.

*Disease and Weakness (Without Death).*—Table VII shows that 10 per cent of the children irradiated in utero exhibited weakness or evidence of disease at birth. No statistics are available that might be used as a standard with which to compare this morbidity rate of the children irradiated while in utero. However, a study of the various

TABLE VI. POSTCONCEPTION IRRADIATION

	NUMBER	PER CENT
<i>Deaths:</i>		
Full-term pregnancies	74	
Deaths	5	100.0
<i>Causes:</i>		
Obstetric	3	6.7
Dystocia	2	
Prematurity	1	
Disease	1	
Pneumonia (2½ months)	1	
Intussusception (2½ years)	1	

disturbances observed would seem to indicate that the irradiation was not a factor in their production. This conclusion is reached because of the wide variety of disturbances noted, and because, in many instances, the conditions were such as are frequently found among children of non-irradiated mothers.

TABLE VII. POSTCONCEPTION IRRADIATION

	NUMBER	PER CENT
<i>Disease and Weakness (Without Death):</i>		
Full-term pregnancies	74	
Disease or weakness	8	100.0
Underweight	5	10.8
Below par mentally and physically	1	
Transient bald spot on head	1	
Transient nystagmus	1	

*Gross Deformities.*—Table VIII presents a group of interesting figures. The most striking fact brought out in this table is the extremely high frequency of mental abnormalities and other disturbances of the central nervous system. Furthermore, a large number of these deviations are of the same type, namely, idiocy of the microcephalic variety. The gross deformities found among the children irradiated while in utero averaged approximately 33 per cent. The extremely high frequency of lesions of the central nervous system, and their conformity to a type, with mental disturbances predominating, would strongly

TABLE VIII. POSTCONCEPTION IRRADIATION

	NUMBER	PER CENT
<i>Gross Deformities:</i>		
Full-term pregnancies	74	
Deformed children	25	100.0
Microcephaly	17	33.7
Hydrocephalus	2	
Mongolian idiot (diagnostic x-ray)	1	
Blind and underweight	1	
Malformation of head	1	
Deformed upper extremities	1	
Spina bifida and double clubfeet	1	
Divergent squint	1	

suggest a common etiologic factor. Since the irradiation is the only influence common to them all that can be recognized, it would seem reasonable to believe that this form of treatment was responsible for the occurrence of these disturbances. According to Doll,<sup>2</sup> microcephaly as a form of idiocy is rare. According to his estimates, it probably does not occur more often than once in every 10,000 or 20,000 births. The fact that 17 instances (23 per cent) of this form of idiocy were observed in the present small number of births (76) in which maternal postconception irradiation was employed is strong evidence that it had its origin in the previous maternal and embryonic irradiation.

*Frequency of Health Disturbances (Postconception Irradiation).—*Fig. 7 shows the relative frequencies of the various health and developmental disturbances observed among the children born after both pre- and postconception maternal pelvic irradiation.

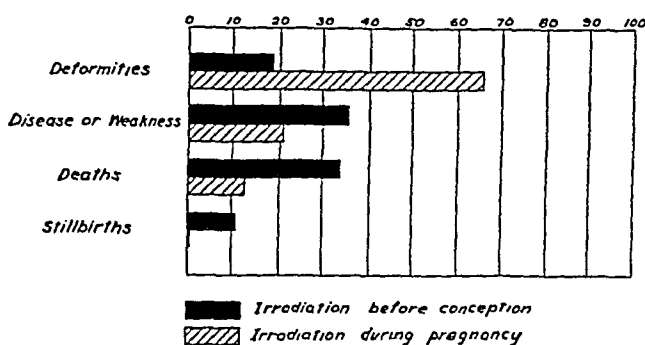


Fig. 7.—Classified health disturbances of children, arranged according to maternal treatment time. Showing the percentage frequency with which the various child health disturbances appeared among the 76 children born following pre- and post-conception maternal pelvic irradiation, arranged according to the time of the maternal treatment with respect to conception. Note the extremely high frequency of deformities observed among the children irradiated during pregnancy.

The most striking fact brought out from the study of this illustration is the extremely high frequency of gross deformities as observed among the offspring of the women receiving postconception irradiation. This fact is the one important observation to be made concerning the influence of postconception irradiation upon the health of the children irradiated in utero. The frequency and uniformity of the defects observed, especially when compared with their frequency (as in the case of the microcephalic idiots), seem to present almost conclusive evidence that these children suffered because of their irradiation while in utero.

*Subsequent Studies Dealing With Unhealthy Children.*—Additional studies on the unhealthy children discussed in this communication are being made. Those making observations have been requested to send in detailed reports concerning their knowledge of these children and all circumstances surrounding the treatment of the mothers. When all available information bearing upon the health of these individuals,

children and mothers, has been secured, an attempt will be made to correlate such data as are available, in order to determine to what extent, factors other than the irradiation may have influenced the health or development of the children concerned.

#### SUMMARY AND CONCLUSIONS

1. Six hundred and twenty-five pregnancies in women subjected to pelvic irradiation treatment have been studied to ascertain the influence of the irradiation upon the length of pregnancy and upon the health and development of the subsequent children.

2. Irradiation *before conception* may be followed by the birth of unhealthy or defective children. It cannot definitely be stated that such maternal treatment has a detrimental influence on the health of subsequent children.

3. *Irradiation of the pregnant woman is extremely likely to be followed by the birth of seriously defective offspring.* The frequency of these defects and their conformity to a type, of which microcephaly is the most common, strongly suggest that they are the result of the irradiation received by the embryos in utero.

4. It is believed that diagnostic curettage should always precede pelvic radiotherapy, in order to avoid possible irradiation of a growing embryo.

5. The conclusion is reached that the pregnant uterus should never be subjected to radiotherapeutic exposures.

6. It is further deemed advisable that should a growing embryo unwittingly be irradiated and its existence later be discovered, such a pregnancy should be terminated at the earliest possible moment.

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- (1) *DeLee, J. B.*: Personal communication to author. (2) *Doll, Edgar, A.*: Personal communication to author. (3) *Falk, I. S.*: *The Principles of Vital Statistics*, 1923, Philadelphia, W. B. Saunders Co., p. 258. (4) *Murphy, D. P.*: *Surg. Gynec. Obst.* 47: 201-215, 1928. (5) *Idem*: *Surg. Gynec. Obst.* 48: 766-779, 1929.

(For discussion, see page 288.)

## THE KEY FIBROID\*

BY EMIL RIES, M.D., CHICAGO, ILL.

*Professor of Gynecology, Post-Graduate Medical School*

OPERATIONS for large and multiple fibroids of the uterus are frequently characterized by difficult approach to the uterine arteries. The management of these arteries is decisive for the speedy and safe performance of such operations. As soon as the exposure of the arteries to sight and manipulation is secured, the rest of the operation becomes not materially different from the course commonly followed in simple operations for fibroids.

Frequently, there are just one or, more rarely, two tumors in the entire mass which prevent easy access to the vessels. As soon as this tumor or tumors are out of the way, the operation which at first appears appallingly difficult or quite impossible, at once becomes simple. The key to the entire difficulty is offered in this particular tumor or tumors. This tumor may therefore be called the "key fibroid."

The key fibroid is found particularly in three different locations, and the earlier in the operation it is found out which of many tumors present is the key fibroid, the more the operation becomes rationalized and simplified. The three types which I have met with particularly are: (1) the intraligamentary fibroid, (2) the cervical fibroid, (3) the adherent culdesac fibroid. Each type demands different treatment.

In the intraligamentary type the peritoneal covering has to be split and detached more or less extensively, while the endangered neighboring organs (rectum, bladder, ureter) have to be kept in mind constantly. If splitting the peritoneum does not give enough mobilization, enucleation of the key fibroid sometimes produces surprising progress.

In the cervical fibroid extensive separation from the bladder may not be sufficient to expose the uterine arteries to the needed degree. Then it may be necessary to split this kind of key fibroid in two, and rotate the two halves outward under constant traction. The traction keeps down the hemorrhage and at the same time makes for greater ease in shelling out the tumor from the pelvic connective tissue so that the uterine arteries can be reached.

If the key fibroid is located in the culdesac and adherent in the bottom of the culdesac, it must first be freed from its adhesions by blunt dissection with particular attention to the rectum. Then it usually can be enucleated from the uterus, whereupon the uterus can be rotated forward and pulled upward, and the uterine vessels become more

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\*Read before the Chicago Gynecological Society at a Joint Meeting with the Chicago Medical Society held April 10, 1929.

readily accessible. The posterior surface of the uterus from which the fibroid was enucleated may bleed some, but this hemorrhage is usually easily taken care of during the next steps of the operation by compression and traction on the entire mass.

These three types of key fibroid are liable to occur in combinations, and there are rare occasions where other types may be found. At any rate when an operation for fibroid appears difficult or does not progress easily, it is always advisable to look carefully for the source of the difficulty which will usually be found in the "key fibroid."

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## MICROCEPHALIC IDIOCY FOLLOWING RADIUM THERAPY FOR UTERINE CANCER DURING PREGNANCY\*

By LEOPOLD GOLDSTEIN, M.D., AND DOUGLAS P. MURPHY, M.D.,  
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**M**ICROCEPHALIC idiocy, as a distinct entity, is a rare condition.<sup>4</sup> Probably not more than one out of every hundred idiots is microcephalic.<sup>2</sup> Nevertheless, it appears to be the most common, single, developmental disturbance observed in children born following therapeutic postconception pelvic irradiation by either radium or the roentgen ray.<sup>4</sup>

The present case of microcephalic idiocy, occurring after postconception radium therapy, is being reported for several reasons. Heretofore, few such cases have been recorded. The child described in this communication has been observed for a longer time than any of the microcephalic idiots previously reported. We have been able to secure exceptionally complete records of the physical condition of the mother, and of the physical and mental development of the child. It is also an interesting fact that this is the second case of microcephalic idiocy occurring after irradiation for carcinoma of the cervix complicating pregnancy, to be reported. The first case observed was reported by Petenyi.<sup>5</sup>

### REVIEW OF THE LITERATURE

During the past year, the Gynecean Hospital Institute of Gynecologic Research of the University of Pennsylvania has been studying the effect of ovarian irradiation upon the health and development of subsequent children. From a review of the literature on ovarian irradiation,<sup>4</sup> and from the data contained in the replies to 1700 questionnaires which were sent to leading gynecologists and radiologists throughout

\*Read before the Obstetrical Society of Philadelphia, Stated Meeting, January 3, 1929.



the United States, 106 women can be reported who had received irradiation therapy during pregnancy. Seventy-four of these women were delivered of full-term children. Thirty-eight of these children (51 per cent) presented disturbances of health or development of a more or less serious nature. In this group, there appeared an exceptionally high incidence of grave mental and gross anatomic defects. Among these 38 unhealthy and defective children, born after postconception irradiation therapy, 16 microcephalic idiotic children were found. Fifteen of these children were born of women who received radium or x-ray treatment early in pregnancy. The case reported by Petenyi, and the one here reported, occurred after irradiation in the latter part of pregnancy.

*Case Report.*—Mrs. C. S., was born in West Virginia, and of Irish descent, entered the University of Pennsylvania Hospital at the age of twenty-nine, on May 12, 1916, for treatment of metrorrhagia. At this time she received radium therapy for a carcinoma of the cervix, and was found to be pregnant.

The patient and her husband both came from large families. There was no history of alcoholism, insanity, or other mental or physical defects in either the patient's or her husband's family. The mentality of the child's mother and father was normal.

The mother has had only two pregnancies. The first resulted in a full-term female child, born in March, 1914. This child has developed normally and is now fourteen years old. With the exception of being underweight, she is physically and mentally well developed, and stands high in her scholastic work. The other pregnancy occurred twenty-six months later and resulted in the microcephalic idiot, which is now being reported.

The mother had always been in good health prior to the onset of her vaginal bleeding.

The patient until the onset of metrorrhagia, had never suffered any menstrual disorder. After the birth of the first child in March, 1914, the patient had lactation amenorrhea for two years. Menses were entirely absent from the birth of the first child until January, 1916, when the patient commenced to bleed. For four months there was irregular bleeding, then the bleeding became continuous. She then entered the University Hospital for treatment on the service of Dr. Floyd E. Keene, through whose courtesy we have been able to make this report.

There were no symptoms referable to the gastrointestinal tract, cardiovascular system, or respiratory organs.

General examination was negative, except for signs of a six months' pregnancy. Fetal movements were active. Springing from the left side of the cervix was a pedunculated, soft, friable, and ulcerated mass about two inches in diameter. The cervix was soft and closed. The uterus was enlarged corresponding to the size of a six months' gestation. The adnexa were normal. A clinical diagnosis of papillary carcinoma, second stage was made, (Schmitz classification).

The blood count showed R.B.C. 3,400,000, W.B.C. 8,000, and Hb. 66 per cent.

The tumor was removed by cauterization, and 185 mg. of radium, filtered with 1 mm. brass and 0.5 mm. aluminum, were inserted at the site of the growth and allowed to remain for twenty-four hours (4440 mg., hr.). The postoperative period was uneventful. There was only a slight rise in temperature and no further bleeding. The patient was discharged on May 29, 1916, in an improved condition. The pregnancy had not been disturbed and the fetal movements were vigorous at the time of the patient's discharge.

A pathologic examination was made by Dr. Charles C. Norris, who reported as follows:

*Macroscopic Description.*—The specimen consisted of an oval mass of grayish, rather soft, friable tissue measuring 6.5 by 5 by 2.5 cm. The surface was irregular and somewhat papillary.

*Histologic Diagnosis.*—Carcinoma cervicis (squamous cell).

*Obstetric History.*—On June 21, 1916, the patient entered the maternity ward of the University Hospital at the onset of labor. The abdomen was enlarged to the size of a seven months' pregnancy, the uterus extending to a level of 3 cm. above the navel. The fetal back was felt to the right; the head was below. The fetal heart rate was 144 per minute.

*Vaginal Examination* showed a scar and crater on the left side of the cervix, the result of the irradiation. The cervix was somewhat dilated.

The first pains began at 8 P.M. on June 21. The membranes ruptured spontaneously at 3:45 A.M. the following morning and the baby was born spontaneously at 4:15 A.M. with the vertex presenting, after a labor of eight hours. The puerperium was uneventful. There was no fever and the patient was discharged on July 12, 1916. On July 16, about two months after the first irradiation, the patient was readmitted and given a second exposure of 85 mg. of radium for twenty-four hours at the site of the cervical scar.

*Present Condition.*—The mother is well at the present time and has no pains or bleeding whatsoever. On May 1, 1917, on examination by Dr. Floyd E. Keene, there was found a moderate atrophy of the vagina with a dense scar at the left vaginal fornix. On rectal examination, there was a marked induration of the left uterosacral ligament. Menses commenced about six or eight months after the last radium treatment on July 16, 1916, and recurred regularly every twenty-eight days until June, 1927, when they ceased entirely. On September 13, 1928, Dr. Floyd E. Keene examined the patient again and found atresia of the upper portion of the vagina with no evidence of malignancy.

The child at birth weighed 2 pounds and 14 ounces and showed no gross abnormalities and no asphyxia, but was about six weeks premature. Lactation amenorrhea, which preceded the pregnancy, made calculation of the exact fetal age impossible. The head measurements, which were all smaller than those of a normal full-term child, were as follows: Biparietal diameter, 8.0 cm.; bitemporal diameter, 6.5 cm.; fronto-occipital, 9.5 cm.; mento-occipital, 10.0 cm.; and trachelobregmatic, 8.0 cm. Other data are lacking concerning the child's condition during its stay at the hospital.

For the first six weeks of life, the baby kept his eyes closed most of the time and had to be fed artificially. Dentition began at nine months. The child could not walk until the age of five years and had to be wheeled in a carriage. Since then he has learned to walk, but trips very easily and falls often. He has never learned to talk, although numerous attempts were made to teach him. His parents have trained him to obey very simple commands such as "sit down," "come here," but these have to be repeated several times. He can make known a few wants to his parents entirely by means of gestures. His general behavior has always been good. He cannot dress or wash himself. There is no history of convulsions, spasms, or twitchings. He was never seriously ill.

The boy at the time of this report was twelve years of age, underweight (60 pounds) and poorly developed. His height was somewhat under normal for his age. Organically, the boy was normal. The parietal and occipital regions of his head were both flattened. He had a fixed and almost vacant facial expression. He could walk but not in a vigorous manner. He held the trunk rather rigidly and his long thin arms were usually held rigidly in partial flexion at the elbow.

His genitalia were normally developed for his age. The Wassermann reaction was negative.

A psychologic examination, by Dr. Edwin B. Twitmeyer at the Psychological clinic of the University of Pennsylvania, showed the following:

*Head Measurements.*—The head was noticeably small, having a circumference of 48.8 cm. (the normal circumference at twelve years was 53.3 cm.). This placed him inferior to the lowest 25 per cent of five year old boys. The cephalic index, the breadth of the skull multiplied by 100 and divided by its length, is 77, which is dolichocephalic in type, close to mesocephalic.

*Mentality Tests.*—Three trials to complete the Witmer-Formboard resulted as follows: The first and second trials were almost satisfactorily completed in three minutes thirty-two seconds, and two minutes twenty-five seconds, respectively. He



Fig. 1.—Photograph of a microcephalic idiotic child, born subsequent to postconception therapeutic pelvic radium irradiation for carcinoma of the cervix uteri. Note the general muscular underdevelopment and the catatonic position of the arms.

failed completely at the third trial. The first and second trials placed him inferior to the lowest 1 per cent of ten year males. He also failed to comprehend the Witmer cylinders, standardized at six years. This failure placed him in the lowest 10 per cent of ten year old males.

The performance tests were poor. Movements were jerky and one hand was used the greater part of the time. Poor analytical discrimination and distribution of attention were displayed. Persistence of attention was good. If made to work under pressure, confusion resulted and results were poorer. This was seen in the third trial of the Witmer-Formboard, when he was urged to hurry.

Because he lacked speech with the exception of repeating the numbers "one" and "two," it was impossible to obtain an auditory memory span. The normal auditory memory span at the age of ten year level for males is the repeating of

six numbers on first trial. If asked to repeat the number "two," he would say "one," and if asked to say "one," he might say "one" or "two." He never said more than one number and invariably it was the wrong one.

Because of language deficiency it was impossible to determine his rating on the Binet-Simon intelligence tests, Stanford Revisions.

*Diagnosis.*—The performance, language, and competency were that of a typical low grade idiot, untrainable and unteachable, and of the microcephalic (conspicuously platycephalic) type.

*Neurologic Examination* by Dr. W. B. Cadwalader was as follows:

The facial muscles contracted equally and normally on the two sides. The tongue appeared to be normal. The upper limbs were slightly rigid, but could be moved passively without difficulty. The biceps and triceps reflexes were very difficult to elicit, because of muscular rigidity, but were equal and slightly exaggerated. Either the right or left upper limb was held in a catatonic position by the patient, where-



Fig. 2.—Roentgenogram of the skull of the microcephalic idiot showing the flattening of the occipital region.

ever the examiner placed it (Fig. 1). Muscular power of the arms and legs were about equal to the muscular development, but the movements were awkward though not severely incoordinate. On passive movement, especially on flexion, the muscles of both lower limbs were slightly spastic. The patellar reflexes were equal and moderately exaggerated. Irritation of the sole of the right foot sometimes caused plantar flexion of the toes, but at other times, a distinct upward movement of the great toe characteristic of the Babinski sign, was seen. On irritation of the sole of the left foot, there was always plantar flexion but a distinct Babinski sign could not be found. The cremasteric reflexes were active and normal. Sensation for pin point appears to be normally felt throughout the body and limbs but the latent period was slightly prolonged. No other forms of sensation could be tested because of the mentality of the patient. The child was certainly imbecilic and the awkwardness of the movement of the limbs, etc., were characteristic of the lack of cerebral development. There was no evidence of deformity of the feet, such as occurs in Friedreich's ataxia or the Charcot-Marie Tooth form of muscular atrophy. The muscular wasting was uniform, not localized, therefore, it was unlike any

form of spinal muscular atrophy. So far as clinical examination was concerned, this case did not seem to be different from other cases of microcephalic idiocy.

*Diagnosis.*—Microcephalic idiocy.

*Ophthalmologic Examination* made by Dr. Edward A. Shumway, was as follows: The eyeballs were of normal size with a moderate amount of catarrh of the conjunctiva, which probably was the cause of the squinting and narrowing of the fissures of the eyelids, as it was apt to cause sensitiveness to light. The ocular rotations were normal and the pupils were equal and responded to light. It is impossible because of the mental condition of the child to obtain any functional tests. The eye-grounds showed clear media, with optic nerves of normal color and sharp outline. The retina and choroid showed no lesions, the eyes were well-developed, and the vision was probably good.

*X-ray Examination.*—Dr. E. P. Pendergrass of the X-ray Department, University Hospital, reported as follows: There was nothing unusual in the head except that it was of the microcephalous type. The pituitary fossa was within normal limits (Fig. 2).

#### DISCUSSION

The possibility that postconception pelvic irradiation can produce cerebral arrest in the embryo is emphasized by numerous experiments reported in the literature. One of us<sup>4</sup> in a recent review of the experimental animal evidence bearing upon ovarian irradiation, drew the conclusion that "irradiation of the developing embryo was extremely likely to injure its health and future development."

It has also been shown that the brains of very young animals are inhibited in their development and may be severely damaged by the roentgen ray. The cerebral defects experimentally produced in newborn animals may well be compared with the arrested cerebral development that followed irradiation of the intrauterine fetus in the case reported in this paper.

Irradiation experiments upon the brains of young dogs have been reported by Brunner,<sup>1</sup> and Krukenberg.<sup>3</sup> The former irradiated the heads of four young dogs from a large litter on the fourth day after birth, with small doses of hard filtered roentgen rays. Ten to fourteen days later, the irradiated animals were found to be backward in growth, and exhibited epileptiform convulsions. Microscopic sections of the brains of these four dogs showed high grade cellular swelling. Krukenberg x-rayed two dogs, one over the fore part, and the other over the hind part of the body. The first dog, irradiated over the fore part, developed poorly during the following two months, and could not walk properly or feed himself. His head and eyes remained smaller than those of a normal dog of the same age. He had suffered from a cerebral defect, as shown by his ataxia, tremor, and visual disturbances. The second dog, irradiated over the hind part, developed normally.

An exhaustive study of our case has been made in order to determine, if possible, whether any relationship exists between the maternal irradiation and the arrested mental and physical development of this child, as it is of great interest to know if the irradiation was the cause of the cerebral defect. The records of the sixteen reported cases of microcephalic idiocy<sup>4</sup> seem to point to irradiation as the cause of the cerebral arrest. If such a relationship exists (and the present study

seems to confirm the conclusions drawn by the authors of the previously recorded cases), then it is always extremely important to consider carefully the possible danger of producing mental or other defects in offspring if pelvic irradiation therapy is employed during pregnancy.

The frequency of microcephalic idiocy, in the children born after irradiation therapy given in the early months of pregnancy,<sup>4</sup> seems to indicate clearly that the irradiation was the causative factor. The case reported by Petenyi<sup>5</sup> of a three months' old, imbecilic, microcephalic child, that was born after roentgen therapy in the fifth and sixth months of pregnancy for carcinoma of the cervix, and the case reported in this paper, both indicate the probability of fetal damage as a result of pelvic x-ray or radium therapy when given late in pregnancy.

This potential danger of ovarian irradiation given during pregnancy necessitates a consideration of the question of artificially interrupting such a pregnancy in order to prevent the birth of a mentally or anatomically defective child. The existence of such a serious complication as a uterine carcinoma or a bleeding myoma during gestation makes the question of the therapeutic procedure to be employed extremely important. Both the welfare of the mother and the health of the fetus must be considered before administering any type of treatment. If irradiation is the treatment of choice, the likelihood of fetal damage should be seriously considered. The circumstances surrounding each individual case deserve careful study and consideration. Basing our views on the frequency of microcephalic idiocy after postconception pelvic irradiation and upon the condition of the child described in this report, we are of the opinion *that no pregnancy should be allowed to continue to term when such radium or roentgen therapy has been employed.*

The value of deep radium therapy for cancer of the cervix in a young pregnant woman is shown in this case report. Complete cure resulted from the employment of 6480 milligram-hours of radium given in two treatments. Another interesting feature of this case is that an artificial menopause was not produced by the large amount of irradiation employed. The patient has had regular menses from 1917 (after eight months of amenorrhea) until her normal menopause, at the age of forty years, in June, 1927, or for a period of eleven years.

The circumstances surrounding the case of microcephalic idiocy described here strongly suggest the conclusion that the cerebral arrest was due to the fetal irradiation.

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THIRTY-FOURTH AND SPRUCE STREETS.

(For discussion, see page 281.)

# LEUCORRHEA, WITH SPECIAL REFERENCE TO TRICHOMONAS VAGINALIS\*

BY CARL HENRY DAVIS, M.D., MILWAUKEE, WISCONSIN

**L** EUCORRHEA is a fairly common complaint. A review of 1000 histories of gynecologic and obstetric patients indicates that about 33 per cent of my patients have some type of leucorrhea. It varies greatly in consistency and amount, but a considerable number of women must wear a sanitary napkin at all times. The occurrence of a more or less frequent, or a constant vaginal discharge, sufficient in amount to keep the external genitalia moist and soil the underclothing is abnormal and requires careful investigation.

The cause as well as the source of an abnormal discharge must be investigated before it is possible to institute a rational treatment. A systematic consideration of this problem is possible only if we list its causes and associated conditions. For convenience they may be tabulated under four headings: (a) parasitic and infective; (b) local; (c) constitutional; and (d) circulatory.

Infective and parasitic conditions which have been found in the genital tract include the following:

Venereal diseases	{ Gonococcus Spirocheta pallida Ducrey's bacillus
Pyogenic bacteria	{ Staphylococcus Streptococcus B. coli Pneumococcus
Micrococcus catarrhalis	
Vincent's bacillus	
Saprophytes	
Rare infections	{ B. tuberculosis B. aerogenes capsulatus B. diphtheria B. tetanus B. typhosus
Protozoal infections	{ Trichomonas vaginalis Ameba urogenitalis
Vermian infections	{ Oxyuris Ascaris Echinococcus Filaria Bancrofti
Thrush, oïdium albicans	
Streptothrix infections, Actinomyces	

\*Read at a meeting of the Chicago Gynecological Society, November 16, 1928.

Infection of the genital tract with any of the above would produce an abnormal discharge.

#### LOCAL CAUSES

Conditions within the genital tract which are associated with more or less leucorrhea include the following:

Endocervicitis	Endometrioma
Cervicitis	Senile vaginitis
Cervical ectropion and erosion	Senile endometritis
Lacerations of the cervix	Cancer of cervix
Polypi	Cancer of corpus
Vaginitis	Sarcoma
Uterine retrodisplacements	Syphilis of cervix
Uterine subinvolution	Tuberculosis of cervix
Foreign bodies	Tuberculosis of endometrium
Chemical irritants	Tubal disease
Adenomas	Fistulas

Bacteria or parasites may be associated with any of the above in the production of the abnormal discharge. Several causes may coexist and an evaluation of their relative importance is necessary before starting treatment.

Constitutional predisposing causes are the anemias including chlorosis and pernicious anemia; endocrine disturbances, and debilitating infections.

A leucorrhea occurring as a complication of the above may not yield to the ordinary methods of treatment unless the constitutional condition is improved.

Circulatory causes include cardiac disease with vascular stasis, and hepatic disease with portal stasis.

Pelvic congestion is a natural result of the above circulatory disturbances. A chronic pelvic congestion will cause some discharge and may greatly increase an existing discharge.

Leucorrhea is an objective expression of a diseased condition. The patient is entitled to a carefully taken history and a complete physical examination. A blood count may show some form of anemia. The urine should be tested. The general examination may reveal a circulatory or constitutional predisposing cause. The local examination should be thorough. While infected cervical glands may be the source of the discharge in a majority of the cases seen in private practice, all other sources must be kept in mind during the examination. Smears and cultures from the urethra, vagina, and cervix should be made whenever indicated. I have found that the examination of the fresh secretion is very important. It is difficult to find parasites such as the *Trichomonas vaginalis* unless the fresh vaginal secretion is diluted with normal salt solution and examined before it dries.



It may be difficult at times to determine the source of the discharge. One of my patients thought she had incontinence of urine when she developed serous discharge from a malignant growth in the uterus. A dry tampon was introduced into the vaginal vault and a few hours later it was possible to convince her that she did not have incontinence. The dry tampon as recommended by Schultze, is also useful in determining whether the discharge comes from the cervix or vagina. The cervical discharge is mucoid or mucopurulent and usually stringy. A discharge coming from the vaginal wall is serous and more uniform in consistency. Usually it is thin and milky. In the presence of marked pelvic congestion white curds may be formed by the mixing of a serous discharge with a large number of epithelial cells. This is most often seen during pregnancy. A watery discharge is an earlier sign of cancer than hemorrhage.

The literature contains many excellent papers on leucorrhea. A number of these have been presented before this society. The bacteriology of vaginal discharges has been carefully studied by Arthur Curtis. The value of the electric cautery and various operative procedures have been discussed in various papers during recent years. However, practically every writer on the subject has admitted that some cases did not respond to the usual methods of treatment, or promptly relapsed when treatment was discontinued. It is evident that most observers in the past have not examined fresh secretions, being content to rely on dried or stained smears.

A few writers including De Lee and Greenhill have urged the importance of examining fresh secretion for the *Trichomonas vaginalis*, but most gynecologists evidently believe this parasite to be an accidental finding and not the cause of vaginitis. Only a few writers have made any reference to it and papers on *Trichomonas vaginalis* usually are limited to clinical observations and methods of treatment. Continued lack of interest in this parasite suggests that gynecologists as a group have not accepted these clinical observations. Prior to January, 1928, I rarely examined the fresh vaginal secretions and had found the *Trichomonas vaginalis* in only a few cases. While writing a chapter on leucorrhea for the *Nelson Loose Leaf Surgery*, I became convinced that the diluted fresh secretion should be examined in every case. About this time a patient whom I had treated periodically for several years returned with a severe vaginitis. *Trichomonas vaginalis* were found in large numbers and the vaginal mucosa presented a typical picture. With adequate treatment the parasites disappeared and she has been free from leucorrhea for nine months. Three patients who had a history of marked leucorrhea for seven years or longer have remained cured for more than six months. During the first ten months of 1928 we have diagnosed *Trichomonas vaginalis* leucorrhea in 38 private patients. Clinical observations on these pa-

tients indicate that a persistent vaginal discharge which causes an irritation of the vagina and external genitalia is frequently due to the *Trichomonas vaginalis*. In several instances a mistaken diagnosis of chronic gonorrhea had been made elsewhere.

#### TRICHOMONAS VAGINALIS

Donné in 1837 observed that a flagellate parasite is present in certain vaginal secretions. This organism has been found by more recent observers in a rather high percentage of persistent abnormal vaginal discharges. (Hausman 40 per cent, Hoehne 28 per cent, Witte 40 per cent, Hegner 50 per cent, Schmid and Kamniker 69.9 per cent.) Brumpt found this flagellate in the vaginal secretions of 10 per cent of the women examined at a gynecologic clinic in Paris.

The life history of the *Trichomonas vaginalis* has never been worked out. Does it multiply only by simple cell division or is there some type of sexual reproduction? How does it survive under unfavorable conditions? Does it form spores? How do women become infected with this parasite? Is it identical with the flagellate found in the intestinal tract? Do patients with *Trichomonas vaginalis* have an intestinal infection as well? None of these questions can be answered at the present time. In a number of cases the vaginitis started under conditions which suggested some relation to coitus and gonorrhea was suspected.

An experimental study of the *Trichomonas vaginalis* is only possible if one can successfully cultivate them in the laboratory. With the cooperation of our bacteriologist at Columbia Hospital, Miss Charlotte Colwell, a laboratory study was started in February, 1928. Our first cultures were made in nutrient broth which was slightly more acid than usual (Lynch). Ordinary glucose broth, glucose brain broth, and nutrient brain broth in deep tubes were used, both plain and with the addition of a few red blood corpuscles. While there was a survival of the flagellates for forty-eight hours and longer, repeated attempts at subcultures failed. There was no apparent increase in the number of organisms in the original culture. Both of these facts indicate survival of implanted organisms rather than growth. We next tried a serum-saline-citrate medium which has been used by Dr. R. W. Hegner of Johns Hopkins for cultivating *Trichomonas hominis*. Repeated attempts with strains from different patients resulted in failure. Locke's solution enriched with ascitic fluid, and Locke egg media were also tried with no evidence of growth.

The first encouraging results were obtained with Locke's solution containing approximately 5 per cent of human blood. The same amount of plain human serum was substituted for the whole human blood because the debris left at the bottom of the culture tube, from the breaking down of the red blood cells, made it difficult to see the flagellates. Experience has taught us that the serum should be relatively fresh. When it is more than one week old growth is not obtained as a rule. Subcultures were made every third day by transplanting approximately 0.1 c.c. of material from the bottom of the tube where the organisms are present in greatest numbers.

Later experience showed that growth is most rapid in glucose broth with 5 per cent human serum, possibly because it is more nutritious. Organisms retain their motility longest in tubes containing 15 to 20 c.c. of medium, possibly because of the

fact that the accumulation of waste products is not as rapid. Twenty-four hour incubation at 37° C. usually produces an active growth. The flagellates may be seen in all stages of simple cell division. They are always most numerous at the bottom of the tube.

Tubes of glucose serum broth whose  $P_H$  varied from 5.1 to 9.5 plus, were inoculated from a sixth subculture of *Trichomonas vaginalis*. They grew rapidly in those tubes of medium whose  $P_H$  varied from 5.1 to 8.5; but there was no evidence of growth in the tube whose  $P_H$  was 8.9; and in the medium with a  $P_H$  of 9.5 the implanted organisms died. It would seem, therefore, that the *Trichomonas vaginalis* grows best in a medium with a reaction similar to human blood.

The treatment of *Trichomonas vaginalis* vaginitis, heretofore has been empirical, and some of the measures used were probably of little or no value. After successfully cultivating this parasite we tried to evaluate the various drugs which have been used in the treatment of leucorrhea by direct toxicity tests under the microscope. The following method was employed: A small loop of culture medium containing a large number of active trichomonas was placed on a slide and a like amount of the solution to be tested mixed with it. The results are easily observed. (The parasite containing medium must be obtained from the bottom of the culture tube by means of a pipette.)

*Effect of various aqueous dilutions of several germicides on Trichomonas vaginalis.*

Control: Activity retained in distilled water for 15 minutes.

*Gentian Violet*:  
1-1000: No motility after 30 seconds. (0.1%)  
1-10,000: Few active organisms after 15 minutes. (0.01%)

*Mercurochrome*:  
1-100: Only an occasional organism retains motion. (1%) after 2 minutes. No motility after 3 minutes.  
1-50: Slight motility after 15 seconds. (2%) No motility after 45 seconds.  
1-20: No motility after 15 seconds. (5%)

*Glycerine*:  
Full strength: Immediate loss of motion.  
50% Immediate loss of motion.  
10% No motility after 1 minute.  
1% Motility marked after 15 minutes.

*Methylene Blue*:  
1-100: Slight motility after 15 minutes (1%).  
1-1000: Active motility after 15 minutes (0.1%).

*Alcohol*:  
Absolute: Immediate loss of motion.  
70% Immediate loss of motion.  
50% Immediate loss of motion.  
25% Immediate loss of motion.  
10% Motility retained after 15 minutes.

*Copper Sulphate*:  
5% Very slight motion after 5 minutes. No motion after 8 minutes.  
1% Motility marked after 15 minutes.

*Lactic Acid*:  
2% Motility ceases after 45 seconds.  
½% No motility after 2 minutes, 40 seconds.

*Lugol's Sol*:  
Instant killing effect in dilutions up to 1-100. (1%)  
1-200: An occasional organism in middle of clumps (0.5%) retains motility for 5 minutes.

<i>Bichloride:</i>	1-1000: Immediate loss of motility
	1-5000: Immediate loss of motility
<i>Lysol:</i>	1-100: Kills instantly, breaking down organisms.
	1-400: Kills instantly, breaking down organisms.
	1-1000: No motility after 3 minutes.
<i>Potassium permanganate:</i>	1-1000: No motility after 30 seconds
	1-5000: No motility after 30 seconds
<i>Metaphen:</i>	1-500: No motility after 1¼ minutes.
<i>Green Soap:</i>	Full strength: Kills instantly. Organisms disappear.
	50% Kills instantly. Organisms disappear.
	25% Kills instantly. Organisms disappear.
	10% Kills instantly. Organisms disappear.
	1% Stops motion instantly. Organisms disappear in 30 seconds.
	0.1% Stops motion in 1 minute. Organisms disappear in 2 minutes.
<i>Sodium Hydroxide:</i>	N/100 Motility slightly impaired after 15 minutes.
	N/10 Motility ceases in 30 seconds.
<i>Silver Nitrate:</i>	5% Immediate loss of motility.
	2% Immediate loss of motility.
	1% Motility ceases after 3 minutes.
<i>Alum:</i>	Equal parts
<i>Zinc Sulphate:</i>	1 teasp. of mixture in } Motility ceases in 2 minutes.
	1000 c.c. of water }
<i>Alum:</i>	1 teasp. in 1000 c.c. water. Very slight motility after 15 minutes.
<i>Zinc Sulphate:</i>	1 teasp. in 1000 c.c. water. Slight motility after 15 minutes.

## TREATMENT

The treatment of leucorrhœa may be divided into a consideration of measures which may give temporary relief of acute symptoms and those which are directed toward the removal of the underlying cause.

*Acute Cases.*—Measures for the temporary relief of acute infections are based on the principle of cleanliness. A cleansing, nonirritating irrigation administered by a nurse is soothing and may be beneficial, but in general I do not favor the use of an internal douche by the patient. The external genitalia should be kept clean with liquid soap and water. Sitz baths afford great relief in acute conditions and may be used several times each day. During the acute stage of any infection rest in bed is essential. The same principles of treatment are applicable to every acute infection with the exception of the *Spirocheta pallida*. As soon as the acute stage has passed a clean speculum of suitable size may be introduced and the vagina carefully dried with sterile cotton pledgets. Following this the entire vaginal mucosa may be painted with a nonirritating antiseptic. I use 5 per cent mercuriochrome or compound tincture benzoin more often than silver salts or iodine. Medicated tampons are of questionable value in most cases and may do harm by withholding the discharge.

*Chronic Cases.*—Satisfactory treatment of chronic leucorrhea depends on removal of the underlying cause. Tampons and douches are of doubtful value and their use is rarely advised.

Chronic endocervicitis is probably the most common cause of chronic leucorrhea. As a rule this may be corrected by means of the electrocautery treatment which I have discussed in other papers.

Surgical removal of the diseased cervical glands is indicated in some cases. This is best done by the Sturmdorf or the Schroeder technic.

The possibility of discharge from Skene's ducts or the Bartholin glands must be kept in mind. These may be destroyed by a fine tipped cautery. However surgical removal of the chronically infected Bartholin glands may give more satisfactory results.

*Treatment of Trichomonas Vaginalis Vaginitis.*—Theoretically it should be possible to destroy all the *Trichomonas vaginalis* in a single thorough treatment of the vagina. However, in practice this is not the case. It seems probable that some of these parasites may be harbored under the inflamed mucous membrane or elsewhere in the genital tract. I have frequently suspected the cervical canal, but thus far it has not been possible to prove that it is responsible for the frequent reappearance of the flagellates after a menstrual period. In obstinate cases I am now using a long thin cautery blade in the cervical canal. It is too early to report results.

Experience indicates that no type of treatment thus far tried will cure every case. It is important that we avoid the use of drugs which will injure the vaginal mucosa. Treatments should be administered at least four times each week and continued until the vaginal mucosa has healed, and pus cells and parasites have disappeared. Daily treatments are advisable in some cases. The following plan is being tried at present:

1. A Miller speculum of proper size is inserted and the vagina dried with cotton; cleansed with 1 per cent lysol solution and again dried.
2. Entire vaginal mucosa is painted with 5 per cent mercurochrome.
3. Glycerine or ichthylol (5 per cent) in glycerine and a tampon is inserted.
4. When a douche is advised either 1 per cent lactic acid or lysol may be used. It would appear that lactic acid has its chief value after the vaginitis has entirely disappeared.
5. A drying powder is at times effective. Kaolin is hard to remove from the vagina and appears to have no advantage over an alkaline mixture such as Bi-So-Dol.

In view of the possibility of an associated intestinal infection the patient should cleanse the external genitalia and anus with liquid soap and water morning and night during treatment, and before coitus and after defecation for an indefinite period.

It is advisable to examine the vaginal secretions for several months immediately after menstruation.

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141 EAST WISCONSIN AVENUE.

(For discussion, see page 284.)

## EXAMINATION OF THE BLOOD IN THE NEWBORN WITH REFERENCE TO TREATMENT FOR HEMORRHAGE\*

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*From the clinic of the Woman's Hospital*

A COMPARISON of the bleeding time, clotting time, and fragility of the blood of 200 newborn babies was made at the Woman's Hospital to determine if any difference could be noted between the blood of babies born with the aid of forceps or other manipulation and

TABLE I

Ages of Mothers—Oldest 44: Youngest 17: Av'ge 26 years, 2 months  
Para i—130: ii—36: iii—17: iv—8: v—4: vi—2: vii—1: viii—1: xi—1

Normal labors	122:	Longest	43 hr. 25 min.	Shortest	10 min.	Average	10 hr. 30 min.
Low forceps	38:	"	31 hr.	"	4 hr. 10 min.	"	13 hr. 20 min.
Midforceps	22:	"	45 hr. 40 min.	"	3 hr. 25 min.	"	19 hr. 14 min.
Breech	8:	"	28 hr. 40 min.	"	2 hr. 45 min.	"	10 hr.
Version	6:	"	17 hr. 40 min.	"	6 hr. 40 min.	"	12 hr. 40 min.
Cesarean	4:						

\*Read at the meeting of the American Pediatric Society, Washington, D. C., April 30, May 1, 2, 1928.

those delivered without instrumentation. The examination was made a simple one so as to establish a hospital routine that might be made available for babies who have to be given blood and serum injections in cases of hemorrhage or when, by reasons of delay or mechanical pressure in labor, the babies might be regarded as liable to hemorrhagic influences.† Spinal tap and puncture of the superior longitudinal sinus

TABLE II

<i>Normal cases</i>				
Clotting time	Longest 9 min.	Shortest 15 sec.	Av'ge 3 min. 5 sec.	
Bleeding time	" 7 min.	" 10 sec.	" 1 min. 55 sec.	
Frag. began	" 0.475%	" 0.375%	" 0.434%	
Frag. complete	" 0.375%	" 0.2 %	" 0.285%	
<i>Low forceps</i>				
Clotting time	Longest 9 min.	Shortest 1 min. 15 sec.	Av'ge 3 min. 24 sec.	
Bleeding time	" 6 min.	" 20 sec.	" 1 min. 51 sec.	
Frag. began	" 0.475%	" 0.375%	" 0.422%	
Frag. complete	" 0.325%	" 0.2 %	" 0.289%	
<i>Midforceps</i>				
Clotting time	Longest 5 min.	Shortest 30 sec.	Av'ge 2 min. 56 sec.	
Bleeding time	" 4 min. 30 sec.	" 10 sec.	" 1 min. 43 sec.	
Frag. began	" 0.5 %	" 0.325%	" 0.426%	
Frag. complete	" 0.325%	" 0.3 %	" 0.299%	

cannot be done in all babies although these procedures may be essential to complete a record and diagnosis. The figures presented were obtained from over 200 babies and as a few records were incomplete 200 cases were used for computation. The data were obtained by Dr. Dreyfuss and the technicians working with him in the pathologic laboratory. The blood was taken from the heel a few hours after birth and examined at once.

The women whose babies were examined were normal, healthy, young mothers, all of whom had a negative Wassermann and the babies

TABLE III

<i>Breech cases</i>				
Clotting time	Longest 4 min.	Shortest 1 min.	Av'ge 2 min. 38 sec.	
Bleeding time	" 3 min. 30 sec.	" 20 sec.	" 1 min. 46 sec.	
Frag. began	" 0.475%	" 0.4%	" 0.462%	
Frag. complete	" 0.325%	" 0.3%	" 0.276%	
<i>Version cases</i>				
Clotting time	Longest 6 min.	Shortest 15 sec.	Av'ge 3 min. 25 sec.	
Bleeding time	" 3 min. 40 sec.	" 55 sec.	" 1 min 57 sec.	
Frag. began	" 0.450%	" 0.425%	" 0.440%	
Frag. complete	" 0.275%	" 0.250%	" 0.265%	
<i>Cesarean cases</i>				
Clotting time	Longest 3 min. 50 sec.	Shortest 2 min. 20 sec.	Av'ge 3 min. 16 sec.	
Bleeding time	" 1 min. 40 sec.	" 1 min.	" 1 min. 22 sec.	
Frag. began	" 0.450%	" 0.4 %	" 0.425%	
Frag. complete	" 0.350%	" 0.275%	" 0.3 %	

†This latter group is being studied by Dr. H. R. Mixsell and will be reported upon later.

were negative, with one exception, to the same test. The average age of the mothers was about twenty-six years and two months. The babies had an average weight of 7 pounds 9½ ounces, so the calculations are based on normal healthy mothers and babies.

In making the records the notations of the blood examinations were entered on the baby's history sheet and later the histories were

TABLE IV

<i>Normal Case—</i>	
Longest clotting time—9 min.	Frag. began 0.475%
Bleeding time—4 min. 30 sec.	complete 0.3 %
Para-i: Age—21: Nationality—Unknown: Labor time 8 hr. 55 min.	
Baby: Sex—Male: Wassermann—++++: Weight 7 pounds 4 ounces.	
Shortest clotting time—15 sec.	Frag. began 0.425%
Bleeding time—1 min. 5 sec.	complete 0.275%
Para-i: Age—25: Nationality—British: Labor time 8 hr. 45 min.	
Baby: Sex—Female: Wassermann—Negative: Weight 5 pounds 12 ounces.	
Longest bleeding time—7 min.	Frag. began 0.4%
Clotting time—1 min. 30 sec.	complete 0.2%
Para-ii: Age—33: Nationality—Spanish: Labor time 9 hr. 25 min.	
Baby: Sex—Female: Wassermann—Negative: Weight 7 pounds 7 ounces.	
Shortest bleeding time—10 sec.	Frag. began 0.4 %
Clotting time—1 min.	complete 0.275%
Para-i: Age—23: Nationality—American: Labor time 5 hr. 45 min.	
Baby: Sex—Female: Wassermann—Negative: Weight 5 pounds 11 ounces	

scanned to determine pathologic factors that might have influenced the results in the blood examinations.

Before studying the figures it is well to compare the classification of the labors so that influences due to the character of the labors on the blood of the newborn may be tabulated in connection with the observation made.

First: In the normal labors the longest labor was forty-three hours, twenty-five minutes and the baby showed a blood-clotting time of five minutes, forty-five seconds; bleeding time two minutes, thirty seconds;

TABLE V

<i>Low Forceps—</i>	
Longest clotting time—9 min.	Frag. began 0.425%
Longest bleeding time—6 min.	complete 0.250%
Para-i: Age—25: Nationality—American: Labor time 6 hr. 10 min.	
Baby: Sex—Female: Wassermann—Negative: Weight 5 pounds 10½ ounces.	
Shortest clotting time—1 min. 15 sec.	Frag. began 0.4 %
Bleeding time—4 min. 20 sec.	complete 0.225%
Para-ii: Age—27: Nationality—American: Labor time 14 hr. 10 min.	
Baby: Sex—Male: Wassermann—Negative: Weight 8 pounds 8 ounces.	
Shortest bleeding time—20 sec.	Frag. began 0.375%
Clotting time—1 min. 30 sec.	complete 0.3 %
Para-i: Age—27: Nationality—German: Labor time 19 hr. 35 min.	
Baby: Sex—Female: Wassermann—Negative: Weight 7 pounds 15 ounces.	



fragility began at 0.425 per cent, complete at 0.250 per cent. In the shortest labor, ten minutes, the baby showed a blood-clotting time of three minutes, forty seconds; bleeding time one minute, five seconds; fragility began at 0.375 per cent, complete at 0.275 per cent.

Second: In the mid-forceps cases the longest labor was forty-five hours, forty minutes, with the blood of the baby having a clotting time of two minutes, fifty seconds; bleeding time two minutes, twenty seconds; fragility began at 0.450 per cent, complete at 0.3 per cent. In the shortest labor time of this series, three hours, twenty-five minutes, the baby's blood showed as follows: clotting time one minute, ten seconds; bleeding time thirty seconds; fragility began at 0.425 per cent, complete at 0.325 per cent.

TABLE VI

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<i>Midforceps—</i>	
Longest clotting time—5 min.	Frag. began 0.4%
Bleeding time—3 min. 10 sec.	complete 0.275%
Para—i: Nationality—Polish: Age—20: Labor time 14 hr. 35 min.	
Baby: Sex—Female: Wassermann—Negative: Weight 7 pounds 5¾ ounces.	
Shortest clotting time—30 sec.	Frag. began 0.425%
Shortest bleeding time—10 sec.	complete 0.325%
Para—i: Age—32: Nationality—Norwegian: Labor time 8 hr. 30 min.	
Baby: Sex—Female: Wassermann—Not taken: Weight 5 pounds 8 ounces.	
Longest bleeding time—4 min. 30 sec.	Frag. began 0.4 %
Clotting time—2 min. 20 sec.	complete 0.325%
Para—i: Age—24: Nationality—Unknown: Labor time 31 hr. 45 min.	
Baby: Sex—Male: Wassermann—Negative: Weight 9 pounds 2 ounces.	

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Third: In breech, version, and cesarean cases the longest clotting time was six minutes and the longest bleeding time was four minutes, thirty seconds. In the fragility tests, fragility began at 0.450 per cent and was complete at 0.350 per cent.

TABLE VII

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<i>Breech—</i>	
Longest clotting time—4 min.	Frag. began 0.4%
Bleeding time—1 min. 20 sec.	complete 0.250%
Para—i: Age—33: Nationality—Norwegian: Labor time 20 hr. 15 min.	
Baby: Sex—Female: Wassermann—Negative: Weight 7 pounds ¾ ounce.	
Shortest clotting time—1 min.	Frag. began 0.450%
Bleeding time—25 sec.	complete 0.325%
Para—ii: Age—Unknown: Nationality—American: Labor time 9 hr. 15 min.	
Baby: Sex—Female: Wassermann—Negative: Weight 5 pounds 11½ ounces.	
Longest bleeding time—3 min. 30 sec.	Frag. began 0.425%
Clotting time—3 min. 30 sec.	complete 0.275%
Para—iv: Age—35: Nationality—Irish: Labor time—3 hr. 15 min.	
Baby: Sex—Male: Wassermann—Not taken: Weight 9 pounds 7 ounces.	
Shortest bleeding time—20 sec.	Frag. began 0.4%
Clotting time—1 min. 20 sec.	complete 0.275%
Para—iii: Age—35: Nationality—Irish: Labor time—3 hr. 55 min.	
Baby: Sex—Female: Wassermann—Negative: Weight 6 pounds 4 ounces.	

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The results of these tests do not disclose a prolonged bleeding time in babies who were born after long labors nor in the babies born after manipulation, traction and version. Among the normal deliveries one mother had a labor time of forty-three hours, twenty-five minutes. Her baby's clotting time was five minutes, forty-five seconds; bleeding time two minutes, thirty seconds; fragility began at 0.425 per cent and was complete at 0.250 per cent. A short bleeding time of ten seconds was noted in a baby born spontaneously and the same time, ten seconds, was observed in a baby born with the aid of midforceps. Apparently the bleeding time was not increased in instrumental deliveries as shown by the average of forceps, breech, version, and cesarean deliveries, viz., one minute, forty-four seconds.

In using saline solutions for hemolysis it is found that some corpuscles will become lysed with one solution and others not. Usually the strengths of the solutions are 0.425 per cent to 0.350 per cent. Solutions of strengths intermediate between 0.44 per cent to 0.34 per cent cause

TABLE VIII

<i>Version—</i>	
Longest clotting time—6 min.	Frag. began 0.425%
Bleeding time—3 min.	complete 0.3 %
Para—i: Age—35: Nationality—Unknown: Labor time 15 hr. 10 min.	
Baby: Sex—Male: Wassermann—Negative: Weight 8 pounds 10 ounces.	
Shortest clotting time—15 sec.	Frag. began 0.450%
Bleeding time—1 min. 10 sec.	complete 0.275%
Para—i: Age—26: Nationality—Unknown: Labor time 6 hr. 40 min.	
Baby: Sex—Female: Wassermann—Negative: Weight 5 pounds 5 ounces.	
Longest bleeding time—3 min. 40 sec.	Frag. began 0.4 %
Clotting time—3 min. 30 sec.	complete 0.225%
Para—iii: Age—33: Nationality—American: Labor time—17 hr. 35 min.	
Baby: Sex—Male: Wassermann—Not taken: Weight 9 pounds 9¼ ounces.	

TABLE IX

<i>Cesarean—</i>	
Longest clotting time—3 min. 30 sec.	Frag. began 0.425%
Bleeding time—1 min. 15 sec.	complete 0.350%
Para—ii: Age—37: Nationality—American.	
Baby: Sex—Female: Wassermann—Negative: Weight 8 pounds 4½ ounces.	
Shortest clotting time—2 min. 20 sec.	Frag. began 0.425%
Bleeding time—1 min. 40 sec.*	complete 0.3%
Para—i: Age—29: Nationality—Unknown.	
Baby: Sex—Male: Wassermann—Not taken: Weight—not given.	
Longest bleeding time—1 min. 40 sec.*	
Shortest bleeding time—1 min.	Frag. began 0.4 %
Clotting time—3 min. 10 sec.	complete 0.275%
Para—ii: Age—27: Nationality—Irish.	
Baby: Sex—Male: Wassermann—Negative: Weight 7 pounds 11½ ounces.	

\*Same case.

a progressively greater hemolysis. A variation of 0.02 per cent in either direction is not beyond normal limits.

After considering the variations in the figures shown in these examinations, it is not found that the blood of the newborn shows changes after delivery by forceps, version, and other manipulation that can be regarded as abnormal.

3 EAST SIXTY-FIFTH STREET.

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## REPORT OF INVESTIGATIONS TO DETERMINE THE THERAPEUTIC DOSE OF DEXTROSE (d-GLUCOSE) ADMINISTERED INTRAVENOUSLY\*

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IT IS now generally agreed that the intravenous administration of dextrose solution is an important and valuable therapeutic measure in a surprisingly large number of pathologic conditions. Indeed in any serious diseased state nothing could be much more basic or fundamental as supportive treatment than to supply a patient with food and water in such a form and by such a route that these are immediately available to the starved and thirsty tissues.

Thus it is both logical and reasonable to expect that benefits should follow such treatment. That favorable effects have been demonstrated is shown by the widespread present-day use of the intravenous injection of dextrose in every branch of medicine or surgery. Those of us who are interested in obstetrics are especially aware of its application to the toxemias of pregnancy.

Despite the very general utilization of this procedure one exceedingly important question regarding it remains unsettled; namely, the actual therapeutic dose of dextrose administered intravenously. In addition to this a considerable range of differing opinions exists in regard to several related points of lesser importance.

Based on these points the theme of this thesis may be summarized briefly as propounding four main questions: (1) What is the proper amount of dextrose to be injected for full therapeutic effect; and (2) is there a maximum limit which becomes the dividing-line between therapeutic and toxic dosage? (3) What is the concentration or percentage of dextrose solution which is to be preferred; and (4) what is the proper rate of injection?

For the sake of brevity the last two may be considered first.

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\*This study was conducted under the generous provisions of the John C. Oliver Memorial Research Foundation at the above Hospital, and is being continued in its various phases under the direction of the Research Committee of this Foundation.

Read before the Brooklyn Gynecological Society, Brooklyn, April 5, 1929.

## CONCENTRATION OF SOLUTIONS

The most favorable results seem to follow the use of the strongly hypertonic solutions and in general our preference is for the 25 per cent solution. It is suggested that interchange of sugar between blood stream and tissues is more rapid when the more concentrated solutions are used.

Nevertheless the concentration to be selected in a given case must depend on conditions to be met. For example, in pneumonia with a weakened heart muscle it is obvious that the 50 to 25 per cent solutions should be chosen so as not to overload or strain the circulatory system, whereas a patient with peritonitis who is dehydrated from diarrhea or vomiting requires water as well as sugar, so that here a 10 per cent solution may be preferable.

## RATE OF INJECTION

The proper rate of injection is already a fixed matter. No more than 0.8 gm. of dextrose per kilo of body weight per hour should be injected according to the accepted findings of Wilder and Sansum.<sup>1</sup> This is much slower than the rate usually employed in the majority of clinics, but to give it more rapidly causes loss of sugar through the kidneys with proportionate loss of therapeutic effect in direct ratio to the excessive speed of the injection. In actual figures this means that in the average sized adult at least thirty to thirty-five minutes should be taken for every 25 gm. of sugar injected. Usually much more is given in considerably less time with immediate "spill" through the urine and proportionately lost effect. Too rapid an injection has been suggested as an occasional cause of reactions.

## DETERMINATION OF THERAPEUTIC DOSE

This leaves for consideration the question of how much dextrose should be given at a single dose, a point which is surely as necessary to know in this connection as it is about any other drug or therapeutic agent. Underdosage has been the common fault and this, with loss from too rapid administration, may account frequently for lack of results. One never thinks of expecting the same marked effect from one one-hundredth of a grain of morphine as from one-quarter grain solely because it is all morphine, yet in the minds of many, dextrose seems to be merely dextrose, and judgment of its merits is shaped without regard to dosage or proper methods of administration.

It has been shown by Foster<sup>2</sup> and confirmed by others<sup>3, 4</sup> that endogenous insulin production in a normal individual is stimulated by intravenous injections or other ingestion of dextrose solutions. Thalheimer and his coworkers<sup>5</sup> have carried out a brilliant piece of work which demonstrated that this insulin-producing activity of the normal

pancreas can be so overstimulated by prolonging the dextrose injection that hypoglycemic reactions can actually be produced thereby.

Although it seems paradoxical, it may be said in other words that the prolonged injection of dextrose will thus produce hypoglycemia rather than the hyperglycemia which one would ordinarily expect.

Let us quote Thalhimer's account of these experiments: "The slow uniform injection of a 10 per cent solution caused a gradual rise in the blood sugar level during the first hour; but, although the injection continued at the same rate, during the second hour the blood sugar level instead of continuing to increase, as might be expected, showed a gradual decline. Following the injection, the blood sugar went to a lower level than after the (other) rapid injection (with which there was excessive urinary loss) and the hypoglycemic reaction was rather severe, similar to a moderately severe insulin shock. There was a decided uniform-

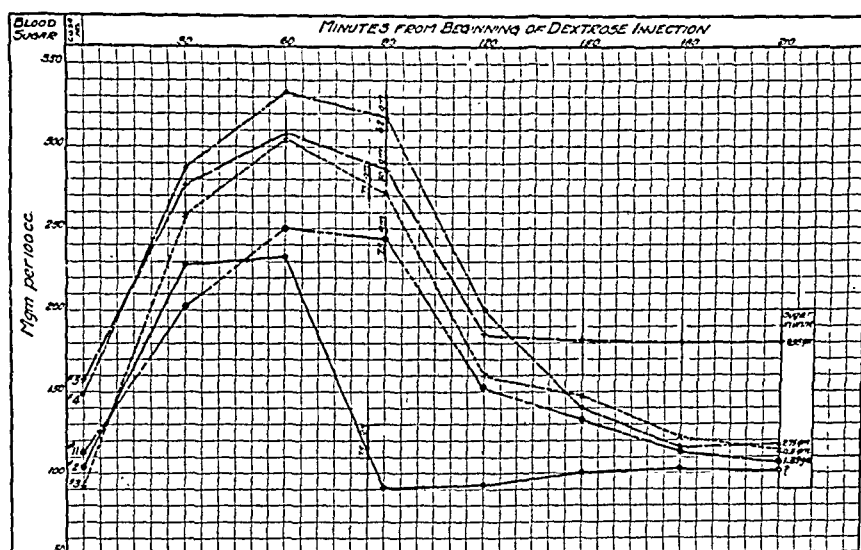


Chart 1.—Glycemic response to intravenous injections of dextrose.

Average female adults; injections at physiologic rate of Wilder and Sansum; all patients uncomplicated or "clean" gynecologic cases, injections immediately following operation.

Each curve represents a separate case study; heavy vertical bars indicate point at which injection ended, figures indicating exact amount of dextrose injected in indicated time.

Cases in this chart show prompt response of pancreas in its insulin-producing capacity as result of sugar injection. Fall in blood sugar at from 60 to 75 gm. dextrose despite influx of injected sugar indicates this to be therapeutic dose.

Further injection would have caused excessive out-pouring of insulin and presently hypoglycemic reaction.

ity in blood sugar curves and urine sugar output in different persons when the same method of administration was used. All showed the decrease of blood sugar during the latter part of the slow administration of dextrose without insulin."

Thalhimer and his colleagues are careful to say that they have not determined that the increased rate of removal of dextrose from the blood is caused by an increased output of insulin but this is a reasonable explanation of the phenomenon they have demonstrated.

This work gave us an idea for a method of determining the thera-

peutic dose of dextrose, since the maximum safe dose should be the desirable dose of this substance.

We reasoned that we might proceed to give an intravenous injection of dextrose solution to an average or normal nondiabetic individual at the rate determined by Wilder and Sansum as being physiologic, so as to insure approximately complete utilization. During this injection we planned to take serial blood-sugar readings and to plot the curves.

According to Thalhimer's previous findings it was to be expected that at first there would be a rise in the curve, then a plateau, after which a fall should begin. This last should represent the point at which the pancreas has begun to show an overstimulation in its insulin-producing function, and at which further injection of dextrose might

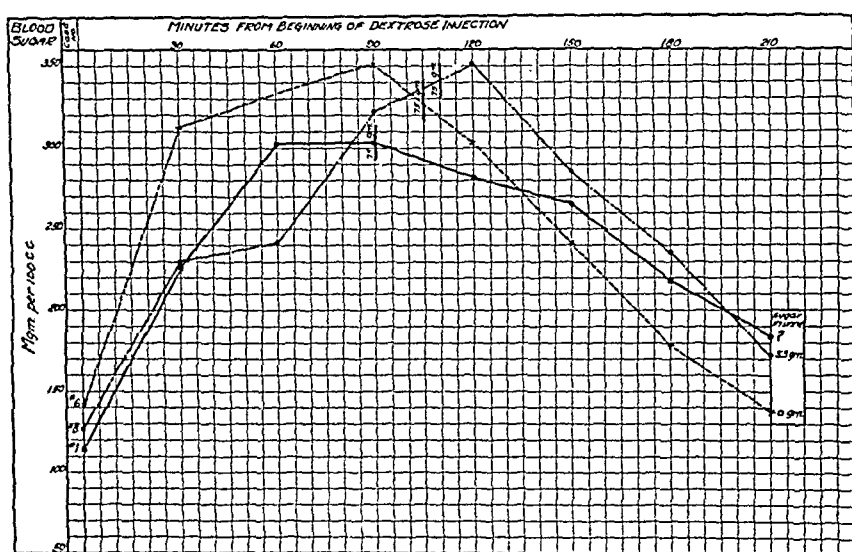


Chart 2.—Same conditions as in Chart 1; same symbols. Slightly slower pancreatic or insulin response to dextrose injections; Cases 1 and 6 being more conclusive than Case 8 that 75 gm. approximates maximum safe dosage.

rapidly become a dangerous matter. To express it otherwise, the amount of dextrose injected up to this point where the blood sugar begins to fall, may be considered as representing the proper amount of dextrose to give for full therapeutic effect. To give more becomes inadvisable and probably has been the source of many dextrose injection "reactions" in the past, these actually being hypoglycemic reactions.<sup>6</sup> On the other hand to give less than this amount keeps the therapeutic effect below its maximum possibility.

The studies based on our plan were conducted as follows: In the Gynecologic Division of this Service it has been our custom for some time past to administer an intravenous injection of 25 per cent dextrose almost routinely following each major operative procedure. This has been done for its action against postoperative nausea and vomiting,

acidosis, and shock, and it may be said that these complications have been reduced thereby to a gratifying minimum.

From previous clinical observation of effects 75 gm. of dextrose (in sufficient water to make 300 c.c.) had been chosen as a single dose, this amount seeming to give the best results. This proved later to be surprisingly close to the correct amount.

These individuals were made the subjects for this study and except for the clean gynecologic operation with its anesthetic which they had just undergone, they were presumably normal adult persons. Blood-

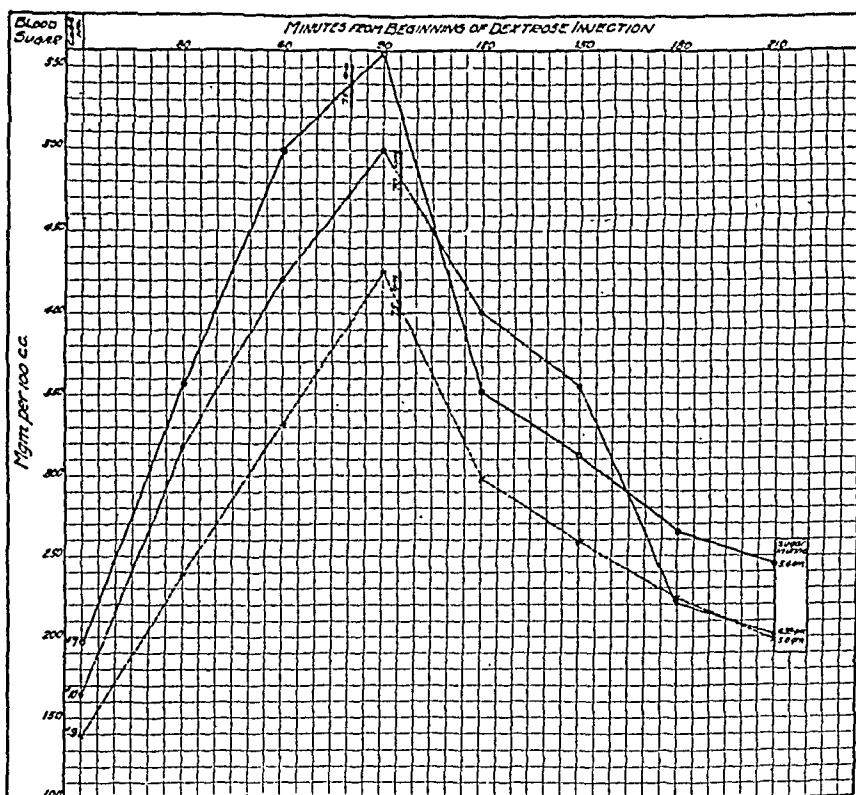


Chart 3.—Same conditions as in Chart 1; same symbols.

Much slower pancreatic or insulin response to dextrose injections with higher levels of blood sugar but prompt subsidence as injection ends.

sugar readings were taken shortly before beginning the injection. The injection was given by means of the infusion apparatus devised in our clinic<sup>7</sup> which accurately regulates the rapidity of the injection to the physiologic rate of Wilder and Sansum. The valve of this instrument varies the flow to the proper speed for whatever strength solution may be chosen. Except for the slight variation from average adult weight by these different individuals the speed of the injection conformed therefore to this correct physiologic rate, thus preventing more than negligible loss of sugar through the urine.

Blood-sugar readings were taken at thirty-minute intervals during

and for a time after the injection and a curve plotted therefrom. Blood-sugar estimations were made by the Folin<sup>8</sup> method and were "uncorrected," normal being considered as ranging from 80 to 100 mg. per 100 c.c. blood. Specimens were examined promptly after collection to avoid deterioration of values. The analysis of urine for sugar was by the Benedict method.<sup>9</sup>

#### EXPERIMENTAL RESULTS

Our results are shown in the charts, and in general these demonstrate two things: that there is a variation in the reaction of various persons to these injections, due probably to individual differences in pancreatic activity or in their sugar tolerance, and second that from 60 to 75 gm. of dextrose are about the maximum amounts which should be administered at a single dose to an average sized adult.

The first of these two conclusions is formed by the observation that the patients in Chart 2 reacted more slowly than those in Chart 1, whereas those in Chart 3 were even less typical, attaining much higher levels of blood sugar than those which we considered more nearly average (Chart 1). Even in this third group, however, there were sharp reactions toward the original levels as the injections were ended.

The second conclusion is fairly apparent from a study of the charts. It will be noted in Chart 1 that the blood-sugar curves had begun to fall before the injection was finished (at from 60 to 75 gm. of injected sugar). In Chart 2 this fall was postponed slightly longer, it being apparent when the analyses came to be made that the drop did not begin until about as the injection was ending.

No further discussion of the metabolic mechanism which is concerned with the rate of disappearance of dextrose from the blood after hyperglycemia need be attempted here. A review of the literature, and the influence of such factors as fasting, action of specific food-stuffs, and medication have been discussed by duVigneaud and Karr.<sup>10</sup> The continuation of the blood sugar to lower than original levels is probably the best proof that endogenous insulin is an influencing factor.

#### SUMMARY

1. Dextrose solution administered by intravenous injection now plays an important rôle as a general therapeutic procedure.
2. Despite the widespread use of this measure adequate observance has not been made of two important points, (1) the preferable concentration or percentage of dextrose solution to be used and (2) the proper rate of its injection.
3. The actual therapeutic dose of dextrose which should be administered intravenously has not been known so that both underdosage and overdosage have been common faults.
4. Individualization of cases must aid in deciding the concentration



of solutions to be injected, but as an average 25 per cent dextrose solution seems to be the most desirable strength.

5. It has been established by previous work that the proper rate of injection into an average sized adult should consume at least thirty to thirty-five minutes for every 25 gm. of dextrose.

6. These present investigations apparently establish the therapeutic intravenous dose of dextrose at 75 gm. for an average sized adult. Less than this will not give the maximum therapeutic effect, and more than this is likely to produce a reaction from overstimulation of the insulin-producing activity of the patient's pancreas. Graphs of blood-sugar curves during dextrose injections show a beginning fall at about this amount thus indicating that the maximum safe limit has been reached.

7. Single intravenous doses of dextrose repeated from one to three times daily as necessary are preferable to prolonged injections for this same reason of excessive endogenous insulin-production. It is likely that many "reactions" attributed to faulty dextrose administration have actually been hypoglycemic reactions from prolonged overdosage with dextrose resulting in overstimulation of the pancreas.

8. By averaging in one's adult patients such variable factors as body weight, individual differences in pancreatic activity, variations in nourishment, and previous medication, it is possible to make a broad statement as to the average routine administration of dextrose. The most beneficial results seem to follow the intravenous administration to an adult of 75 gm. dextrose in a volume of 300 c.c. (25 per cent) during a period of ninety to one hundred minutes. It is suggested that the amount of dextrose thus administered to a half-grown child should be one-half, and to an infant one-quarter of the adult dose but that the same total length of time (ninety to one hundred minutes) should be consumed for these injections. Other concentrations of solution or lesser amounts may be used according to individual requirements but the above represent safe and adequate average standards of dextrose dosage.

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## THE INCIDENCE OF SYPHILIS AMONG PREGNANT NEGRO WOMEN\*

BY C. LEON WILSON, B.S., M.D., CHICAGO, ILL.

ARTICLES on the prevalence of syphilis among Negroes are frequent. This incidence varies widely, apparently, dependent upon the section of the country concerned, and the type of patients seen. Various and sundry reasons have been advanced for this condition none of which we believe to be conclusive. In a search through the literature there was revealed an incidence which varied from 16.6 per cent in a New Orleans clinic to a report by McCord yielding 30 to 35 per cent. In order to determine for himself the exact state of affairs, the author began keeping record on all cases of pregnancy intrusted to him. The work extended over quite a period of time and is presented as a preliminary report, a final report to be made at a subsequent date.

As a routine part of the prenatal care given patients, especially those of negro extraction, a blood Wassermann was taken and results noted. These results were checked in all cases with a Kahn and in some cases with another Wassermann and if there was any element of doubt, the tests were repeated. We might add that the blood was drawn by the author and the specimens sent to one of the most reliable laboratories in the city and in no case did we run the test. During the year 1927 a Wassermann was taken on both mother and child eight weeks following delivery, whether she had received antisyphilitic treatment or not. During this period there were 66 positive tests and at the end of eight weeks 19 of these tests were repeated with the result that 14 were still positive and 5 were negative, and of the infants so tested 2 were positives. About one-half of these 66 cases received specific treatment and the cases noted above belonged to this group.

The negro women were, for the most part of Southern birth and residents of the North for a period varying from two and three months to eight and nine years. They represented the usual type of patient seen in a clinic, and were of average intelligence. Some were of the very highest group who represented training and a knowledge of the comforts and luxuries of life, who wish excellent care but are not disposed to pay for it, some of the group of average citizens who have a desire for the best things of life and good care and attention during this period and who are unable to pay for same and others of that large group who, because of economic conditions and ignorance, are

\*Read before the Physicians Association of Cook County, May, 1928.

forced to seek charity. Hence, our figures are taken from a cross-section of negro life and practically all classes are considered. The ages of mothers ranged from sixteen to forty years.

In every case our diagnosis of syphilis has been based on a positive blood reaction and not on clinical evidence except in a few instances. This is so, since none had any external evidence of the disease and only a few clinical evidence, judging from their histories of abortions, stillbirths, and the absence of any rash that could possibly be adjudged syphilitic at any time. One fetus showed the characteristics of inherited syphilis although the mother gave no evidence of the disease. Two mothers had had repeated miscarriages, no living children, a positive Wassermann and after receiving six intravenous injections of 0.4 and 0.6 neoarsphenamine gave birth to living children.

The occurrence of miscarriage is not necessarily always due to syphilis. Stokes believes that such terminations of the pregnancy occurring time after time at approximately the same month, usually the third or fourth, are unlikely to be of syphilitic origin. Chronic hypertrophic endometritis, fibroids, and foci of infection, especially teeth, appear to be the greatest causative factor. The teeth of practically all of these women were uniformly bad, the good ones being the exception and could easily account for the number of miscarriages seen. Again another causative factor in this type of patient is the economic element, the struggle for existence where the woman is compelled to be a wage earner and at times do heavy work. These women often are undernourished, in a weakened physical condition, and hence unable to withstand the burden of childbearing.

The work of the last year raises a question in our minds as to the reliability of a Wassermann during pregnancy, since during the year no case so diagnosed yielded any clinical evidence of value of the disease, no child exhibited the stigma, and usually with or without treatment the blood report was negative eight weeks after delivery. As a matter of fact the value of a blood Wassermann during pregnancy has been the subject of much discussion since Grosz and Bunzel in 1909 reported temporary positive tests during eclampsia. Stuhmer and Dreyer are among those who believe that a Wassermann at this time is too uncertain and that its abandonment would cause families less mental and financial worry. Belding estimates that 25 per cent of the positives in pregnant women with cholesterolized antigens may prove nonsyphilitic. McCord believes Wassermann reactions are at this time dependable if properly done. Recently it has been shown that pregnancy is in a way a treatment for syphilis, in that it may reduce the danger of the central nervous system type and that a woman who has gone through pregnancy would show less clinical evidence than one who has not. Stillians is of the opinion that with the Kolmer-Wassermann technic the test is almost as reliable in pregnant

and nonpregnant parturients. Be that as it may we hope to arrive at a more definite conclusion later and with this in mind we have adopted a plan whereby we make the test on all patients eight weeks first after delivery and then three to six months following delivery, whether they have received treatment or not. Belden states that in nonsyphilitic pregnant women a variable positive reaction may result from the anticomplementary action of the serum and from nonsyphilitic fixation. Such reactions are weaker but there exists no means of differentiation between syphilitic and nonsyphilitic fixation in weakly positives.

Our series comprises 3631 cases with positive Wassermanns totalling 272, beginning in 1920 and ending in 1927. The results given are quite different from all other reports and serve to show that in a large number of cases and classes there is no more syphilis among pregnant negro women than any other racial group. In other reports where the incidence is higher, this is probably due to the small number of Negroes seen or that they belong to the lowest intellectual group, or where the economic factor enters. These people when once infected spread the affliction to others, since their income will not admit of continuous and rigorous treatment. Bad housing conditions, where many families are forced to live together in order to meet the high cost of living, account for much of the disease present. In this report all positive reports were included whether or not they were classified as weak positive or strong positive. We feel that it is not safe to disregard a weak positive, for a low titer antigen may have been used and thus not rule out the disease. On the other hand we take no chance with the offspring despite the fact that Cooke and Jean have shown that the chances of a woman with a weak positive giving birth to a healthy child are six or eight to one.

YEAR	CASES	POSITIVE WASSERMANNS	
1920	159	24	
1921	235	28	
1922	292	42	
1923	170	27	
1924	528	33	
1925	375	27	
1926	355	25	
1927	1417	66	
	<hr/> 3631	<hr/> 272	7.49 per cent

Belding states that collected statistics from the South give 30.6 per cent positive for the Negro. He again states that positive Wassermann tests in Boston were 9.4 per cent for second generation American, 16 per cent for Negro, and 7.7 per cent for Russian Jew. He believes that according to birthplace the foreign and northern Negroes yield an incidence of 10 per cent, Southern 27.1 per cent. But we show an incidence with, as previously stated, practically all of the cases studied

being from all parts of the South. All other observers report an incidence varying from 16 to 25 per cent.

A brief comparison of the two races, white and black, is shown in the following table.

POSITIVE WASSERMANN REACTION IN PREGNANT WOMEN

AUTHOR	YEAR	CASES	PLACE	PER CENT POSITIVE
Commisky	1916	1822	New York City	8.0
Ottensburg	1917	2488	Sloane Maternity	9.9
Williams	1920	4000	John Hopkins (White)	2.5
			" " (Col.)	16.3
Welz and Van Nest	1922	699	Detroit Charity (White)	5.7
		786	" " (Col.)	19.3

Those with positive Wassermanns were given antisyphilitic treatment. The number of injections varied from one to twelve, one patient receiving 22 injections. The dose varied from 0.3 to 0.45, 1.6 neoarsphenamine. One patient developed a dermatitis, and one albumin in the urine.

During 1927 when there were 1417 cases and only 66 positive Wassermanns, we attempted to keep close watch on all positives. The report shows that of these 66 cases, 3 gave clinical evidences of the disease and of 135 previous pregnancies in these women, there were three premature deliveries and of these three, one woman had a delivery at seven months and two, abortions at two and three months, one had one labor at seven months, and the other two at seven and eight months. There were 21 abortions divided as follows: one had two at three months, one at two months and premature at seven months and one had four at five months, one had three abortions all others ranged from one to three months and the cause was usually given as unknown or due to a fall or strain. The other instrumental delivery was due to a generally contracted pelvis. As to the present pregnancy there was one prematurely born twins, one abortion and

COMPARISON OF PREVIOUS AND PRESENT PREGNANCIES OF 66 SYPHILITICS AND NONSYPHILITICS

NUMBER OF CASES 132	66 SYPHILITIC	66 NONSYPHILITIC
Positive Wassermanns	66	0
History of syphilis	0	0
Clinical evidences of syphilis	3	0
Previous pregnancies		
Total number	135	153
Premature (28 to 38 weeks)	3	8
Abortions up to 28 weeks	21	17
Stillbirths after 28 weeks	1	1
Instrumental deliveries	1	0
Wassermann after 8 weeks	14 positive	0
Present pregnancies		
Premature	1 (twins)	0
Abortions	1	0
Stillbirths	1	0
Deaths	0	0
Wassermann after 8 weeks	3	0

one stillbirth. Eight weeks after delivery the Wassermanns were positive in fourteen mothers and two babies.

In the 66 nonsyphilitic cases picked at random, none gave any clinical evidence of the disease, the previous pregnancies totalled 153, 8 ended prematurely. Of this number one had three such labors at four, six, and seven months, but it should be noted that in this case the blood pressure varied from 140 to 175 systolic and 85 to 105 diastolic. The remaining instances had had only one such ending usually at seven and eight months. There were 17 abortions, varying in number from one to three times, three being the average, and one had had an abortion at three months and premature delivery at eight months. Only one stillbirth occurred. Hence, we see there is very little difference in the total pregnancies, between the syphilitic and nonsyphilitic cases. During the current year it is our plan to carry this work further and collect data on treated and untreated positives including an eight-weeks' Wassermann on both mother and infant. Some work of this nature was done this year but the results do not cover a sufficient number of cases to warrant a report at this time.

#### SUMMARY

1. Negro parturient women are alleged to have a high incidence of syphilis.
2. Value of Wassermann during pregnancy is questionable.
3. Out of 3631 cases there resulted an incidence of 7.48 per cent as compared with higher percentages of other authors.
4. In a large number of cases there is little difference between syphilitic and nonsyphilitic women as to the final outcome of the pregnancy.

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306 EAST FORTY-THIRD STREET.

## METAPHEN IN THE TREATMENT OF PUERPERAL SEPTICEMIA AND OTHER BLOOD STREAM INFECTIONS

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DESPITE the fact that numerous substances have been employed in combating septicemia, there has not as yet been developed a drug which yields entirely satisfactory results. Among the chemical compounds which have been most commonly employed are mercurochrome,<sup>1</sup> gentian-violet,<sup>2</sup> neutral acriflavine, rivanol (an acridine derivative), arsphenamine, neoarsphenamine, and Pregl's iodine solution, in addition to sera and blood transfusions. The route by which all of the above substances are administered is the intravenous. At first the results obtained with some of them were very encouraging, but at present they have all been practically abandoned except mercurochrome, either because of their toxic effect upon the patient or on account of their uncertain ability to produce definite curative results.

It has been definitely established that mercury compounds generally exert a very powerful destructive effect upon bacteria in the test tube, more so than most of the known antiseptics. George W. Raiziss of Philadelphia, has also succeeded in synthesizing a valuable organic mercury compound, possessing high bactericidal properties. Its chemical composition indicates that it is 4-nitro-3,5-bisacetoxymercuri-2-cresol. The product is known as metaphen.<sup>\*3, 4</sup> It contains approximately 60 per cent of elemental mercury and is so powerful that it inhibits the growth of staphylococci in a dilution as high as 1:20,000,000. It has been used with gratifying results in surgery and in the treatment of various bacterial infections. That metaphen possesses unusually high bactericidal properties is evident upon comparing the results obtained with it and with mercuric chloride. This superiority is even greater when each of the two mercurials is left in contact with the various microorganisms for more than one hour. The following table indicates the results obtained with these two compounds:

From these results it is apparent that metaphen has a very destructive effect not only upon the cocci, but upon spore bearing bacilli such as *B. anthracis* and *B. subtilis*. In experiments with these two organisms the superiority of metaphen over mercuric chloride and phenol manifests itself to an amazingly high degree: in the case of *B. anthracis* with an exposure of one hour, metaphen is 11 times more germicidal than bichloride of mercury and 2,450 times more so than phenol; in a 4 days' exposure it is 47 times more powerful than mer-

\*The description of its chemical properties and some clinical data concerning its use, can be found under the Section, "New and Non-official Remedies" of the Journal of the American Medical Association, v. 83, p. 1167, Oct. 11, 1924.

DILUTIONS BACTERICIDAL FOR ORGANISMS EXPOSED FOR INDICATED TIME PERIODS

COMPOUND	STREPTOCOCCUS AUREUS		STAPHYLOCOCCUS HEMOLYTICUS		GONOCOCCUS		B. ANTHRACIS		B. SUBTILIS	
	1 hour	4 days	1 hour	4 days	15 min.	30 min.	1 hour	4 days	1 hour	4 days
Metaphen	170,000	3,350,000	90,000	3,140,000	380,000	380,000	326,000	8,000,000	133,000	2,640,000
Bichloride of Mercury	106,000	336,000	125,000	180,000	—	—	29,000	170,000	25,000	103,000
Merurochrome	4,500	36,000	5,300	24,000	56,300	66,300	530	31,000	230	17,000
Phenol	—	—	200	200	333	400	133	1,860	100	290



curic chloride and 4,300 times more so than phenol. In the tests performed with *B. subtilis*, metaphen is 5 times more effective than mercuric chloride and 1,330 times more than phenol with a one hour exposure, while with an exposure of four days the same mercurial is over 25 times more efficient than bichloride and 9,100 times more powerful than phenol.<sup>3, 4</sup>

While experiments *in vitro* afford a more or less definite idea as to the antiseptic or germicidal results obtainable in surface infections, the same is unfortunately not true of blood stream infections. In such cases the effect produced by the intravenous injection of a drug is dependent upon other important factors, such as its organotropism for the host and the extent to which its germicidal action is reduced in the blood stream due to its combining power with the serum proteins. As to the first of these factors, thousands of injections of metaphen have been given without producing harmful effects upon any organ of the body or inducing an immediate reaction, such as rise in temperature, nausea, vomiting, etc. The dose employed is usually 10 c.c. of the 1:1,000 solution; this is given daily, except in those cases where the nature of the infection or the condition of the patient is such as to warrant the use of larger doses, e.g., 20 or 30 c.c. Since metaphen is a mercurial, it is necessary to carefully watch the urine for the first appearance of albumin and casts; under these circumstances the use of metaphen should be temporarily discontinued until the urine is again normal.

An important point in connection with the efficacy of metaphen when administered intravenously is its low affinity for the proteins of the blood. Experiments in a 50 per cent serum medium indicate that it does not form a precipitate in a solution as concentrated as 1:200, whereas with mercuric chloride a precipitate is formed in a final dilution of 1:1,200.

During the past three years metaphen has been administered by the venous route in a number of cases of bacteremia and septicemia with generally satisfactory results. The present author conducted a clinical investigation of the value of this drug in the above types of cases, and the results thus obtained, as well as those of other physicians, totaling 16, are included in the following report. It is important to note that despite the successful results obtained with metaphen, we are as yet unable to explain the mechanism of its curative action. Since the quantity of the drug introduced into the infected blood stream is not large enough to produce complete sterilization directly, it is our belief, therefore, that in addition to its germicidal action upon the organisms present, the drug also exerts an inhibitive effect upon those remaining alive. Possibly also the mercurial is able to stimulate the development of antibodies or to assume the rôle of a foreign protein. But regardless of the exact explanation

of its therapeutic action we nevertheless are of the opinion that, on the basis of the results obtained thus far, the intravenous use of metaphen affords a satisfactory agent for the treatment of blood stream infections.

In injecting the drug we used a needle of 22 gauge and about  $1\frac{1}{4}$  inches in length. After the needle with the syringe attached has been introduced into the vein, it is better to aspirate a quantity of blood into the syringe and then slowly inject the resulting mixture of blood and metaphen. During the injection it is advisable to occasionally aspirate additional quantities of blood into the syringe and then reinject until all of the metaphen has thus been introduced. In this way we have managed to avoid the development of phlebitis after the injection.

#### CASE REPORTS\*

CASE 1.—Female, A. M. For the past five years the patient has been suffering with pain in the back and a heavy bearing down pain. About one year ago she began having headaches (frontal) and dizzy spells. A week ago severe pain was felt in the left side, accompanied by light fever, nausea and vomiting. She had not been able to eat anything for the past week. On the day previous to admission she had marked dysuria.

The patient was admitted to the hospital on August 14, 1927 with a large tubo-ovarian abscess, and during the following four weeks her temperature ranged from 100 to 102° F. At the end of this time 10 c.c. of metaphen 1:1,000 were injected intravenously. Within a few hours the temperature dropped to normal and remained so for two days. No untoward reaction was observed. The temperature then oscillated between normal and 100° during the next five days, when a second injection of 10 c.c. of metaphen 1:1,000 was given. Again the temperature dropped to normal and remained so for the next two days. On the third day after this injection an operation was performed.

A large tuboovarian abscess was drained through the abdomen. The patient ran a high temperature for nine days afterward but the wound kept draining satisfactorily. Finally, the temperature gradually decreased to normal and remained so; accordingly, she was discharged on the twentieth postoperative day.

CASE 2.—Male, Mr. O. Diagnosis. Osteomyelitis of one foot. Repeated examination of the blood gave positive results for *Staphylococcus albus*. The patient was very sick and steadily grew worse. Death was expected at any time, but still he refused to allow an amputation to be performed.

As a last resort four doses (10 c.c. each) of metaphen 1:1,000 were given intravenously. The condition of the patient improved, and though he still had a draining osteomyelitis of the foot, he was well enough to leave the hospital, and was in good condition otherwise.

CASE 3.—Female, R. R. Complained of generalized abdominal pain and vaginal bleeding. She had developed an apparent generalized peritonitis following uterine manipulation after a self-induced abortion. Her temperature was fairly constant around 103°.

On the second day after admission to the hospital (October 20, 1927) she was

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\*The first 8 cases are from the author's own practice; the remaining 8 were reported to Dr. George W. Raiziss by various observers whose permission to publish them, has been obtained. On this occasion, we express our sincerest appreciation to those who have submitted the reports.

given an intravenous injection of 10 c.c. of metaphen 1:1,000 and there resulted a breaking of the temperature followed by a great alleviation of symptoms. The temperature, however, continued to oscillate between 100 and 102°.

On October 27, 1927 a pelvic abscess, which had formed, was incised and a T-tube drain inserted. The patient made an uneventful recovery and was discharged about three weeks later.

CASE 4.—Female, E. S., aged twenty-four years. Complained of dizziness and edema of feet, painful micturition followed by a burning sensation. A Wassermann taken at this time (January 23, 1928) was negative. The blood pressure was 114/78. On Feb. 27, 1928 the urine was clear, alkaline in reaction and had a sp. gr. of 1.020; on March 12, 1928 it was acid in reaction, showed a faint trace of albumin and a trace of sugar, and the sp. gr., was 1.012. The patient had her last normal menstrual flow in July, 1927 (length ten days), although on December 16 there was a scanty flow for three days.

She was admitted to the maternity ward on April 1, 1928, at 2:15 A.M. and at 8 A.M. of the same day, the baby was born spontaneously with no lacerations. The following day there was evident a slight elevation of temperature; on the next day it began to rise until on the third day it was round 104° and thenceforth rarely went below 101°. Pulse ranged between 120 and 130; respiration between 32 and 36. Two injections of metaphen (10 c.c. each) were given, the first on April 8 and the second on the eleventh. No reaction occurred at any time during or after the injections. The temperature dropped to normal within forty-eight hours after the last injection; the same was true of the respiration and pulse. She was discharged on April 14 in good condition.

CASE 5.—Female, L. H., aged twenty-two years. Appeared on Oct. 26, 1927, complaining of slight nausea, constipation and frequency of urination. Urine at that time was clear, acid in reaction, sp. gr. 1.001 and otherwise negative. The blood Wassermann reaction was negative. She had had her last menstrual period on July 14, 1927; it lasted one and one-half days as compared to the usual flow of three days' duration.

The patient was admitted to the maternity ward at 10:30 A.M. on April 6, 1928. The baby was born at 8:27 P.M. on the same day spontaneously and with no lacerations. The placenta was delivered spontaneously. On April 8 (two days after delivery), the temperature went up to 104° and remained there, rarely going below 101°. Her pulse was around 140 and respiration between 28 and 40. Three injections of metaphen 1:1,000 (each 10 c.c.) were given at forty-eight hour intervals. Two days later the pulse and respiration became normal. No reaction was noticed at any time during or after the injections.

Patient was discharged on the nineteenth. She was still weak and undernourished but was much improved. Examination revealed a mass on the right adnexa which was probably the cause of her trouble.

Urine examination on the ninth of April showed a trace of albumin, acid reaction, sp. gr. 1.010. Blood count which was taken on the sixth showed: hemoglobin 75 per cent; red blood cells 3,320,000; white blood cells 10,300; color index 0.98 plus. Another leucocyte count taken on the ninth showed 9,500. Blood pressure ranged from 88/50 to 100/70.

CASE 6.—Female, M. U., aged twenty-four years. On Sept. 12, 1927 complained of backache, bleeding, and constipation. Complications which developed were acute pyelitis and moderate nausea and vomiting. Blood pressure at this time was 110/50. Urinalysis showed a distinct trace of albumin, acid reaction, sp. gr. 1.019 and positive acetone; otherwise negative. Blood count was as follows: hemoglobin 67; red blood cells 3,550,000; white blood cells 13,400; color index 0.94.

The patient was first admitted to the maternity ward on September 13 with a

history of frequency of urination, chills, and severe pains in the loins, particularly the right one, radiating anteriorly into the abdomen. She had a high fever, ranging from  $102^{\circ}$  to  $104^{\circ}$  for seven days, which dropped to normal for a few days, then rose again to  $102^{\circ}$  and  $103^{\circ}$  and remained there fairly constantly. Her pulse varied from 110 to 140 and at one time went up to 160. Respiration ranged from 20 to 40, averaging about 30. At the time the temperature was normal, an abscessed tooth was removed, but after this a relapse of symptoms occurred and her condition remained about the same (temperature ranged between  $102^{\circ}$  and  $104^{\circ}$ ). The patient decided to sign a release and go home, but just before she left she was given an injection of 10 c.c. of metaphen 1:1,000. On returning one week later she informed us that her temperature had dropped the next day after the injection. In addition, there was a gradual disappearance of pus in the urine and an absence of all symptoms and signs. The temperature remained normal until delivery.

The patient was followed by our prenatal clinic until time of delivery, when she was admitted to the maternity ward on January 28 at 1:45 A.M. The baby was born at 4:34 P.M. on January 29, with spontaneous mechanism and no lacerations. Immediately after delivery the temperature rose to  $101^{\circ}$  and  $102^{\circ}$  and remained at this point for three days. Metaphen was given intravenously and the temperature declined to normal. Moreover, the pulse, which was about 97 on admission and rose to 120 after delivery, slowly came down to normal after the administration of metaphen. Respiration ranged between 20 and 24. Patient improved very nicely and was discharged on February 8 in good condition.

A blood count taken on January 30 showed the following: hemoglobin 68; red blood cells 3,250,000; white blood cells 8,200; color index 0.87. The urine showed a trace of albumin, acid reaction and sp. gr. 1.010.

CASE 7.—Female, R. S., aged thirty-nine years. Suffered from pain in the small of the back radiating to each flank. Her temperature was  $104^{\circ}$ . General examination was negative; there was tenderness over both kidney areas and some rigidity over the upper part of both recti; chest, pelvic joints, spine, and extremities were all negative.

Blood count taken on March 20, 1928, showed the following: hemoglobin 73 per cent; red blood cells 4,050,000; white blood cells 8,400; color index 0.9.

Urine was acid in reaction from 3/31 to 4/4 and then became alkaline; albumin ranged from a distinct trace to a very faint trace and a large amount of pus was present. Urine culture on 4/4 showed *Bacillus coli communis*.

On April 2, 10 c.c. of metaphen 1:1,000 was injected intravenously. No reaction occurred. On April 4 the temperature was normal, and since the patient felt well, she was discharged on April 14 in good condition.

CASE 8.—Female, M. W., aged thirty-eight years. Developed a chill four days after normal delivery (Aug. 8, 1928). During the next twenty-four hours her temperature rose to  $101^{\circ}$  F., and then returned to normal; while on the succeeding day the temperature gradually rose again to  $102.4^{\circ}$  and then continued to fluctuate between  $103^{\circ}$  and  $99^{\circ}$ . On Aug. 11, 1928, an injection of metaphen was given (10 c.c. of 1:1,000 solution); during the next forty-eight hours the temperature varied from normal to  $101^{\circ}$ . Accordingly, a second injection of metaphen 1:1,000 was given (10 c.c.) on Aug. 13, 1928. During the succeeding twenty-four hours the temperature gradually dropped to normal but thereafter it again began to fluctuate between normal and  $102^{\circ}$ . On Aug. 17, 1928, a third dose of 10 c.c. of 1:1,000 metaphen was administered; the temperature became normal within twelve hours and has remained so to date (Aug. 25, 1928).

The blood count taken on Aug. 11, 1928, prior to the injection of metaphen, showed 22,400 leucocytes, 86 per cent of which were polymorphonuclear cells.

After each dose of metaphen the white cell count diminished until on Aug. 22, 1928, it amounted to 8,400.

No untoward effect was observed after any of the three injections of metaphen.

CASE 9.—A young woman, twenty-eight years of age, aborted two weeks before entering the hospital. She developed a postabortal septicemia. *Streptococcus nonhemolyticus* was recovered in the third blood culture seven days after admission (Oct. 14, 1925). Her temperature showed variations from normal to 104°, 105°, and 106° steadily for one month. She had three blood transfusions on Oct. 15, Oct. 26, and Nov. 6 (each 500 c.c. of citrated blood); four subcutaneous injections (10 c.c. each) of boiled milk on Oct. 22, Oct. 25, Oct. 28, and Oct. 31; three intravenous injections of formalin (0.5 c.c. each) on Nov. 9, Nov. 10, and Nov. 11, with no permanent relief. Finally, the doctor decided to use metaphen intravenously as he believed the patient was about to die. Accordingly, he injected 3 c.c. on Nov. 14, 6 c.c. on Nov. 15, 10 c.c. on Nov. 16 and 10 c.c. on Nov. 17. After the third injection of metaphen the temperature dropped to normal and remained so until Nov. 22 inclusive, after which the patient was allowed to be taken home on Nov. 23. Her temperature has continued to remain normal to date.

CASE 10.—Complete recovery was obtained in a case of puerperal septicemia caused by an infected thrombus in the left uterine wall containing *Staphylococcus albus* and *aureus*. Nineteen intravenous injections of 1:1,000 metaphen (10 c.c. each) were given in twenty-four days, at the end of which time the patient's temperature continued to remain normal and was finally discharged as cured. No reaction or renal irritation was observed at any time.

CASE 11.—Woman, aged thirty years, began to exhibit a temperature varying from 99° and 104° on the fifth day after delivery. Puerperal septicemia developed, due to an infected thrombus in the right uterine wall, containing *Staphylococcus albus* and *aureus*.

Thirteen daily intravenous injections of metaphen 1:1,000 (10 c.c. each) were given. Temperature now continued to remain normal without any fluctuations and complete recovery resulted.

CASE 12.—On March 4, 1927, a patient was treated at the hospital for a postpartum infection, running a temperature of 105°. It has come down to normal. We have given her altogether five injections of 20 c.c. of metaphen intravenously on five consecutive days.

CASE 13.—Two injections of metaphen (20 c.c. each) were given on subsequent days, intravenously, to a patient who had had a very obscure infection with marked venous thrombosis in both arms, but a persistently negative blood culture. She had been running a spiking temperature between 99° and 104° for going on to three weeks. Following these two injections, which were absolutely all one could get into her, her temperature subsided and she was discharged about ten days later.

CASE 14.—Female, aged thirty-five years, developed a postabortal septicemia with positive blood cultures for *Streptococcus nonhemolyticus*. The temperature declined from 104.4° to 100.2°.

She was first given a transfusion of 200 c.c. of citrated blood. The next day, temperature being 100.6°, the contents of 1 ampule of metaphen (10 c.c.) were given intravenously and within twenty-four hours the temperature dropped to normal and remained so until the patient was discharged about a week later.

CASE 15.—Female, aged twenty-eight years, developed septicemia two days after delivery of a stillborn child (Feb. 8, 1927). The temperature rose to 102.6° F., fluctuated between 104° and 100° for the next four days, and between 101° and

normal for the following two days. On Feb. 15, 1927, the patient developed a chill; this was followed by a rise in temperature to  $104.8^{\circ}$  and then a drop to  $99.8^{\circ}$  within twenty-four hours. On Feb. 16, 1927, the temperature rose to  $104.6^{\circ}$ ; 10 c.c. of metaphen, 1:1,000 was injected intravenously. During the next twelve hours the temperature descended to  $99.4^{\circ}$ , and during the following twelve hours it rose to  $105.4^{\circ}$ . A second intravenous injection (10 c.c.) of 1:1,000 metaphen was now given (Feb. 17, 1927). About twelve hours later the temperature had dropped to normal, then rose to  $105.4^{\circ}$  and gradually descended to normal again, where it has remained with but slight fluctuation until the date of discharge (March 3, 1927).

#### DISCUSSION

Case 1 represents septicemia associated with a large tuboovarian abscess. The temperature reached  $102^{\circ}$  F. and remained high during a period of several weeks. The first intravenous injection of metaphen brought the temperature down to normal; later it went up slightly, but the second injection brought it again to normal. Here the drug permitted us to reduce the temperature prior to surgical operation, in this way creating a more favorable condition for surgical intervention. The patient finally recovered.

In the second case, one of osteomyelitis, 4 intravenous injections of metaphen exerted a striking therapeutic effect. In this case, the blood showed positive findings for *Staphylococcus albus*. Death was expected as the patient refused to undergo an operation. The intravenous administration of metaphen improved the patient so that he was able to leave the hospital. Case 3 is similar to Case 1, where the intravenous injections of metaphen brought the temperature down prior to an incision of a pelvic abscess. The intravenous administration of metaphen and surgical intervention brought the case to a complete recovery.

Case 4 represents puerperal septicemia, the temperature rising to  $104^{\circ}$  F. for almost a week. Two intravenous injections of metaphen, without any untoward reactions, brought the temperature abruptly down to normal. A similar drop to normal occurred in the respiration and pulse. The patient recovered. A similar case of puerperal septicemia with a temperature of  $104^{\circ}$  F., high pulse rate and high respiration is evidenced in Case 5. The intravenous injections of metaphen with no untoward reactions, given every other day, brought the temperature, pulse rate and respiration down. The patient was saved.

In Case 6 we have acute pyelitis, high blood pressure, traces of albumin, low hemoglobin and low red blood cells, leucocytes increased to over 13,000. Temperature went up to  $104^{\circ}$  F., and remained for several days at  $103^{\circ}$ ; pulse and respiration were high. One intravenous injection reduced the temperature to normal, followed by disappearance of pus from the urine. The same patient developed high temperature following childbirth. Metaphen was given intravenously and caused the temperature to come down to normal. It is interesting

to note that leucocytes of the blood following intravenous injections of metaphen practically became normal.

In Case 7 with temperature reaching 104° F., we have pyelitis due to *Bacillus coli communis*. One intravenous injection of metaphen caused the temperature to become normal. The patient was subsequently discharged in good condition. In Case 8, a puerperal septicemia with temperature fluctuating between 99° and 103° and blood count showing more than 22,000 leucocytes, three intravenous injections of metaphen brought the temperature to normal and the leucocytes to about 8,000. Case 9 is postabortal septicemia with positive *Streptococcus nonhemolyticus* in the blood. The temperature fluctuated from normal to 106° F. After several remedies were tried the patient was given up and death was expected at any time. After the third intravenous injection of metaphen, the temperature dropped to normal resulting in a complete recovery. In Case 10, we also have puerperal septicemia. Nineteen intravenous injections of metaphen brought the temperature to normal causing complete recovery.

Case 11 is another instance of puerperal septicemia. Here 13 intravenous injections brought about complete recovery. Case 13 is also an instance of puerperal septicemia. Five injections, 20 c.c. each, of metaphen given on five consecutive days saved the patient. Case 14 puerperal septicemia with *Streptococcus nonhemolyticus*, recovered following one intravenous injection of metaphen and blood transfusion. Case 15, puerperal septicemia with very high temperature, was brought under control with 2 intravenous injections of metaphen. The patient recovered.

In metaphen we have a drug of considerable potency and I would not hesitate to say that in blood stream infections it is one of our most valuable agents. It is the least harmful of all drugs which may be injected intravenously but yet it has a definite therapeutic value. The rigors which we were accustomed to see following intravenous medication with certain drugs, are absent. There is an attempt of natural establishment of the patient's equilibrium. Also, the individual's own defensive mechanism is brought into use to fight the invaders. The temperature will drop quite promptly following the injection but not as with other forms of intravenous medication where the pulse rate still remains high. Metaphen causes a corresponding drop in the pulse rate. The patient invariably feels better soon after the injection. Sometimes this period is not permanent and injections have to be repeated. Even if the case has been neglected or the patient does not have the resistance, still metaphen causes some response in such cases. I would like to mention here, that the drug may be administered also in desperate cases without any fear of causing a fatal issue due to the drug itself or its reaction.

Blood counts should be taken before and the day after injections.

We have observed striking changes taking place in the white blood cells, especially the polymorphonuclear leucocytes. Metaphen, when injected into the blood stream of an individual suffering from an acute infection and showing a high white blood cell count, especially the polymorphonuclear leucocytes, causes a decided drop in the white blood cells and a corresponding drop in the polymorphonuclear leucocytes.

The kidneys seem to be quite tolerant to this form of therapy, even repeated doses of metaphen do not seem to irritate the kidneys. It is important to remember that metaphen should not be used as a last resort. As soon as systemic infection is suspected, the patient having had a chill or a persistent elevation of temperature, it is not advisable to wait until the patient is moribund, but the best thing is to start in with the intravenous injections of metaphen. I have tried many times the so-called prophylactic metaphen treatment and I feel sure, that some patients who have only had one injection of metaphen, responded promptly with a resulting drop in temperature and pulse rate. The patients invariably felt better. They might not have fared as well if metaphen had not been used promptly.

Therefore, I will repeat that, when using this drug to prevent the development of septicemia, the feeling of security seems justified due to the low toxicity of metaphen in the doses recommended. If the patient should eventually show that there was no definite serious infection, the injection has not done any harm as far as the general welfare of the patient was concerned. It is my impression that the prophylactic use of metaphen may prevent the development of grave cases of blood stream infection in which often no remedy can save the life of the patient.

#### CONCLUSIONS

1. In sixteen cases of blood stream infection, metaphen injections had a beneficial effect.
2. In the doses recommended, metaphen is of low toxicity. No untoward reactions have been observed following its intravenous administration.
3. In many cases of puerperal septicemia, metaphen brings high temperature, pulse rate and respiration down to normal. Its intravenous administration is recommended as a safe and potent measure in blood stream infections.

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# DIATHERMY AS AN ADJUNCT IN THE TREATMENT OF PELVIC INFLAMMATORY DISEASE\*

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## INTRODUCTORY REMARKS

ALTHOUGH quite recently there has been a tendency to advocate early surgical intervention in inflammatory cases, the period of watchful waiting is firmly established in our management of these conditions.<sup>1</sup> The value of lengthy observation and conservative measures is twofold: First, if sufficient time is allowed to elapse, nature, judiciously aided, will restore the diseased parts to normal in many instances. Secondly, surgery, if eventually required, is adaptable as a means of overcoming the sequelae of the acute condition, and can be conservatively employed.

The importance of conservatism cannot be overestimated, and it is incumbent upon us to be receptive to such innovations as may prove to be effective adjuncts. Rest is of paramount importance, combined of course with proper hygienic and dietetic measures. Heat, in the form of prolonged vaginal douching is of proved value, while the intramuscular injection of foreign protein, either as boiled milk or in the form of one of its refined products, has merited a place in the management of properly selected cases.

## THEORIES AND PREVIOUS INVESTIGATIONS

The value of heat in the cure of disease has been recognized since the earliest days of the art of medicine. In most cases, the normal body temperature is ideal for the growth of germs, and any elevation from this point has a deterrent effect on the growth and vitality of each bacteria. The temperature necessary to destroy bacteria is usually quite high, and some bacteria or their spores can resist high temperature for a considerable time. Even the gonococcus, which is considered to be quite easily destroyed by slight elevation of temperature has upon investigation by Schofield<sup>2</sup> been found to resist a temperature of 109.4° F. for thirty minutes, and in some instances, 111.2° F. for the same period of time. When we consider that the limit of toleration for normal cells without damage has been placed at 116° to 118° F., it can be seen that even the disease germ with the lowest thermal susceptibility is very close to the temperature that will damage the normal tis-

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sue. The hope of sterilizing germs in normal tissue by temperature alone would seem therefore to be doubtful of accomplishment.

Another factor, seemingly the most important one, is the increase of circulation brought about by the application of heat. The increased blood supply brings to the part additional leucocytes and antitoxin to neutralize the poisons. If we have succeeded in increasing the temperature only a slight degree, the attenuated organism falls an easier victim to the phagocytic attack, and the return circulation aids in prompt elimination.

Thus, while the increased temperature is a factor, the greater aid comes from the increased blood supply. Another point that must be borne in mind is that every slight increase in temperature means a marked increase of chemical action and metabolism. This latter action is not only local, but the functional activities of the organs of elimination are increased thereby.

When we consider diathermy as an agent in the production of increased heat and circulation, we find that much has been written about the ability of the high frequency current to increase the temperature of the tissues. It has been claimed in some instances that an increase of from 5 to 10° has been attained (Binger and Christie<sup>3</sup>). Theoretically this is possible in some instances, but so many factors enter into it, that these statements are open to grave doubt. The body has a very efficient heat-regulating mechanism, and local or general increase of temperature calls into play every active effort to dispense and eliminate such heat. The heat, being due to the resistance of the tissue to the passage of the current, will depend to a large extent on the density of the tissue in question, the denser the tissue, the greater being the heat generated. Furthermore, if there is a pathway of lesser resistance, the current will traverse that instead of passing through dense tissue. Important factors, then, are the density of the tissue, and the degree of access and egress of the blood supply, which will tend to disperse the heat very rapidly. In view of these facts, it would seem that diathermy accomplishes results without necessarily increasing the temperature to such an extent as to destroy germs, and that criticism of this method for that reason alone is not sound.

While Gellhorn<sup>4</sup> states that heat ranges of 40 to 50° C. (104 to 122° F.) are produced within the affected tissues themselves, Bettman and Crohn,<sup>5</sup> from a series of carefully conducted experiments, conclude that it seems impossible to focus the site of heat in any given internal viscus; they conclude further that skin effect, which is dependent on relative specific resistance and specific conductivity of tissues, is a factor in keeping the current near the surface of the body. They could not demonstrate experimentally actual localized deep tissue heating and their opinion is that the greatest amount of heating takes place near the electrodes, and that the deeper portions received a pro-

portionately small amount of current. Furthermore, that some specific action of the electric current, apart from the heat generated, may be produced, cannot, they believe, be answered. This work is convincing, and we are inclined to agree with them; it is our belief that it is the circulatory factor, rather than the amount of heat produced in the tissues, that is responsible for whatever good effect diathermy has.

The use of diathermy in the treatment of pelvic inflammatory disease was suggested to us by the favorable results reported by Cherry<sup>6</sup> in a study of one hundred cases, 72 per cent being cured or improved, a very high percentage. He employed three routes; abdominovaginal, abdominosacral, and abdominorectal, preferring the first named. In addition he treated as foci of infection, the cervix and urethra, using the Corbus thermophore.

A striking feature he noted was almost instant relief of pain in all cases. In those cases operated upon following the use of diathermy, he felt that the structures were more hyperemic, the adhesions vascular and less dense, and that the postoperative convalescence was more satisfactory, with less tendency to wound infection. His experience in postpartum infections was interesting. One, a postpartum case of three weeks' duration, with a moderate pelvic mass, reacted severely with pain, rise in temperature, and resultant pelvic abscess, requiring posterior colpotomy. A second case reacted so severely that death ensued. These calamities he attributed to activation of virulent infection. He reported no experience in the chronic type of postabortal infection.

While impressed with his results in general, we do not agree with his assumption that actual destruction of the gonococci in the deep tissues is brought about by heat penetration.

Dittmer<sup>7</sup> (quoted by Gellhorn<sup>8</sup>) reported 937 cases treated, with subjective cure or improvement in 87 per cent. Lindemann<sup>9</sup> (quoted by Gellhorn<sup>8</sup>), found that operation was greatly facilitated by the prior use of diathermy.

#### SCOPE OF THE INVESTIGATION

This investigation was begun as an unprejudiced attempt to determine the clinical value of diathermy in the treatment of pelvic infection. We have chosen to regard its employment as an adjunct to the recognized methods of treatment, and in no sense as a curative measure alone. The scope of our study was arranged to embrace three phases: First, observations on a series of cases in which the abdominosacral method was used; secondly, treatment of a group by the abdominovaginal method in conjunction with high frequency desiccation of the cervix as a focus of infection; thirdly, the analysis of an equal number of cases in whom no diathermy had been employed.

The cases were selected by one of us from Dr. Anspach's Gynecologic Service at Jefferson Hospital over a period of one year, begin-

ning in November, 1927. In our selection of patients we chose definitely outstanding cases of inflammatory disease, neisserian, post-abortal, or puerperal in origin, excluding complicating myoma uteri, or ovarian tumors. The treatments were carried out by another of us in the Physical Therapy Department, the diagnosis, observation and determination of end-results having been in the hands of the clinician and gynecologist. The final evaluation is free from the bias of the physiotherapist, and is judged by the former in its comparison with a similar series treated by the usual routine methods. Our basic idea being to present clinical data, no human, animal or cadaveric experimentation was performed, relative to the development and conductivity of heat in the tissues. Reference to Bettman and Crohn's article, previously mentioned, is recommended, as well as to the work of Binger and Christie.

#### TECHNIC EMPLOYED

The first series of cases were treated by the abdominosacral method. A block-tin electrode 15 by 20 cm. was placed on the back, in the region of the sacrum. On the abdomen, a kidney-shaped electrode was used, 20 cm. long by 10 cm. wide, narrowing to 6.25 cm. at the center. This electrode was placed over the lower part of the abdomen, to cover the approximate position of the tubes and ovaries, the narrow center corresponding to the position of the uterus. No soapsuds or water were used on the electrodes, allowing the natural moisture of the skin to complete the contact. The current was turned on slowly until the skin became well moistened and gradually increased to tolerance. With the equipment used, the meter usually registered between 1000 and 1200 ma. The treatment was given three times a week, except during menstruation or irregular bleeding, beginning with fifteen minutes the first time and continuing for one-half hour thereafter.

In the abdominovaginal method, the kidney-shaped electrode was used on the lower abdomen, the vaginal electrode being inserted in the vaginal vault behind and against the cervix. The current was employed in a similar fashion, the temperature of the vaginal electrode being measured by a thermometer registering from 101.5° to 102° F. at the maximum.

In the treatment of the cervix as a focus of infection, surgical high frequency was used in the form of the monopolar Oudin current, accurately adjusted to produce a desiccating effect without too deep destruction, and not sufficient to excite a fibrous tissue reaction; the spark short, but fairly intense.

After careful cleansing and drying of the part, the current was first applied around the outer edge, and gradually advanced up into the canal. A slough formed, usually coming away in a few days.

No thermophore treatment of the urethra was employed, nor were Skene's glands treated with high frequency desiccation in any case.

#### ANALYSIS OF THE DIATHERMY GROUP

Table I shows the result of diathermy treatment as employed in 30 cases with respect to the presence or absence of adnexal masses, and their disappearance or reduction.

Table II refers to the results based upon etiology. One unimproved case of puerperal origin was of especial interest. Reacting badly to diathermy, the procedure was discontinued, and for nearly nine months, the patient was treated expectantly. Having no suitable domicile it was necessary to keep her in the hospital. Repeated sedimentation tests showed no improvement in the amount of tissue destruction evidently going on. She repeatedly reacted to pelvic examinations, but finally operation was performed. The pelvis presented an appearance little short of an acute condition, and the operation was technically difficult. Convalescence was complicated by severe wound infection. This was the most refractory case in either series, but she is perfectly well today.

TABLE I. ADNEXAL MASSES, DIATHERMY GROUP

BEFORE TREATMENT	CASES	CURED	IMPROVED	UNIMPROVED
Adnexal Masses Present	25	10-40%	7-28%	8-32%
Absent or Indefinite	5	2-40%	2-40%	1-20%
(One of these cases operated upon.)				
AFTER TREATMENT	CASES	CURED	IMPROVED	UNIMPROVED
Adnexal Masses Disappeared	4-16%	4	-	-
Reduced	13-52%	-	7	6
No Change	8-32%	-	-	8
(7 of these cases operated upon)				

TABLE II. ETIOLOGY, DIATHERMY GROUP

	CASES	CURED	IMPROVED	UNIMPROVED
Neisserian	20	9-45%	4-20%	7-35%
Puerperal or Postabortal	9	3-33.3%	5-55.5%	1-11.1%
Undetermined	1		1	

TABLE III. AGE INCIDENCE, DIATHERMY GROUP

DECADE	CASES	OPERATED UPON
10-20	2-6.6%	
20-30	15-50%	3
30-40	13-43.3%	5

Table III represents the age incidence.

Table IV presents a comparison of the two methods of application. Our experience during the first six months with the abdominosacral method gave us valuable information relative to the selection of cases for diathermy, and that accounts to some extent for the much smaller

group treated by the abdominovaginal route during the second six months. The premises governing this selection of cases will be considered at a further point in the discussion.

Comparative results apparently favor the abdominosacral method. However, the smaller number of cases in one group lessens the value of comparative results. Our feeling is that there is little to choose from in the selection of either method, especially since the value of the treatment depends more on increased circulatory change than upon the development of increased temperature in the tissues themselves.

In those few cases in which the cervix was treated as a focus of infection, we do not feel justified in drawing conclusions as to whether or not the treatment of the focus influenced the pelvic pathology to any extent.

TABLE IV. METHODS OF DIATHERMIC APPLICATION

	ABDOMINOSACRAL	ABDOMINOVAGINAL AND CERVICAL DESICCATION
Number of Cases Treated	24	6
Cured Anatomically or Symptomatically (or both)	10 - 41.6%	2 - 33.3%
Improved	6 - 25%	3 - 50%
Unimproved (operation performed or advised)	8 - 33.3%	1 - 16.6%

Table V exhibits the combined results of treatment by both methods, together with the average number of hospital days. We regarded a case as cured when the symptoms abated, with or without the disappearance of any adnexal masses. Cases were discharged from the hospital after subsidence, and treatment continued in the outpatient department, with examinations at regular intervals until discharged as cured, being instructed to report any recurrence of symptoms. A patient exhibiting any annoyance whatsoever, even though comparatively comfortable, we regarded merely as improved.

TABLE V. RESULTS, DIATHERMY GROUP

		AVERAGE NUMBER OF HOSPITAL DAYS
Number of Cases Treated	30	47
Cured	12 - 40%	34
Improved	9 - 30%	27
Unimproved	9 - 30%	89
(8 of these cases operated upon)		
No mortality in entire series		

TABLE VI. COMPARATIVE STATISTICS

	CHERRY (100 Cases)	DITTMER (937 Cases)	THE AUTHORS (30 Cases)
Cured	42%	40%	40%
Improved	30%	48%	30%
Unimproved	28%	12%	30%

In unimproved cases, operation was advised and performed in all but one instance (refused). Of these cases operated upon, the majority showed pelvic adhesions that were rather readily separated, the operative procedure not being technically difficult. Ovarian conservation, or transplants, were performed in half the cases, complete ablation taking place in four patients, aged thirty-nine, thirty-eight, thirty-two and twenty-seven years respectively. Two of the cases operated upon were of special interest. Both reacted badly to diathermy. One of these showed a complicating fibroid tumor of the uterus, that had not been previously diagnosed. The other was the postabortal case of ten months standing, mentioned earlier in this paper. This was the only case to develop infection of the incision. There was no mortality in the series.

In regard to the hospital days, one case is responsible for the very high average, the postabortal case, previously mentioned as being so refractory to treatment, requiring two hundred and ninety-one days. Excluding this most unusual case, the average for the entire series would have been forty days, and for the unimproved group, sixty-four.

Table VI compares the results of this investigation with those of other observers.

#### ANALYSIS OF THE EXPECTANT TREATMENT GROUP

Thirty cases of pelvic inflammatory disease in whom no diathermy was used were selected from the Gynecologic Service. Patients having complicating conditions, as myoma uteri or ovarian tumors, were excluded as in the diathermy group. The type of cases were practically identical as to symptomatology, pelvic findings, and clinical course, and were all treated within the past two years, the ordinary expectant measures being employed.

Table VII contrasts with Table I, with respect to the disappearance or reduction of adnexal masses.

Table VIII, regarding etiology, contrasts with Table II.

Table IX, age incidence, contrasts with Table III.

Table X compares the results of expectant treatment and the average number of hospital days, with the diathermy results shown in Table V.

Of the operative cases, ovarian conservation or transplant was accomplished in 5, while complete ablation was performed in 3 patients, forty-two, twenty-four, and twenty years of age, respectively. A recurrent case, previously operated upon, was exceedingly difficult, with masses of adhesions, a wound infection resulting. There was, however, no mortality in the series.

Regarding hospital days, in the unimproved group, we were dealing with a number of recurrent cases, which had been observed in the dispensary for some time. Consequently, upon admission to the ward, the waiting time preceding operation was shortened considerably, a decided factor in the lower average number of hospital days shown in Table X as compared with Table V.

TABLE VII. ADNEXAL MASSES, EXPECTANT TREATMENT GROUP

BEFORE TREATMENT	CASES	CURED	IMPROVED	UNIMPROVED
Adnexal masses present	28	12 - 42.8%	9 - 32.1%	7 - 25%
Absent or indefinite	2	1 - 50%	—	1 - 50%
(One of these cases operated upon)				
AFTER TREATMENT	CASES	CURED	IMPROVED	UNIMPROVED
Adnexal masses disappeared	7 - 25%	7	—	—
Reduced	14 - 50%	5	9	—
No change	7 - 25%	—	—	7
(7 of these cases operated upon)				

TABLE VIII. ETIOLOGY, EXPECTANT TREATMENT GROUP

	CASES	CURED	IMPROVED	UNIMPROVED
Neisserian	23	11 - 47.8%	5 - 21.7%	7 - 30.4%
Puerperal or postabortal	5	2 - 40%	3 - 60%	—
Tuberculous	1	—	—	1
Indefinite	1	—	1	—

TABLE IX. AGE INCIDENCE, EXPECTANT TREATMENT GROUP

DECADE	CASES	OPERATED UPON
10 - 20	6 - 20%	—
20 - 30	19 - 63.3%	6
30 - 40	3 - 10%	1
40 - 50	2 - 6.6%	1

TABLE X. RESULTS, EXPECTANT TREATMENT GROUP

		AVERAGE NUMBER OF HOSPITAL DAYS
Number of cases treated	30	28
Cured	13 - 43.3%	24
Improved	9 - 30%	27
Unimproved	8 - 26.6%	33
(All of these cases operated upon)		
No mortality in entire series		

## RÉSUMÉ AND COMMENT

A résumé of the cases treated without diathermy, in comparison with the group in which it was employed, brings to light some interesting observations.

There was little variation in the proportion of cases exhibiting adnexal masses, as shown in either series.

The percentage of improvement, considered upon an etiologic basis, is practically the same in both series, with those of neisserian origin largely in the majority.



In both series the preponderance of cases occurred in the second decade. Of the cases coming to operation, the majority were between thirty and forty in the diathermy group, while the majority were between twenty and thirty in the expectant treatment group. It is interesting to note that ovarian conservation or transplants could not be accomplished in 2 patients, of twenty-four and twenty years, respectively, in the expectant treatment group. On the other hand, in the group receiving diathermy, only one patient, twenty-seven years of age, could not have ovarian conservation practiced.

The most striking comparison is found in the percentage of cures, improvement, and in the average number of hospital days. The figures practically parallel each other as regards cure and improvement, 70 to 73 per cent.

When we consider the average number of hospital days, however, the cases in whom diathermy was not used, assuredly spent less time in the hospital. As mentioned in a previous paragraph, a single case, decidedly resistant to diathermy and in whom its use was discontinued, is responsible for the very high average number of days in the unimproved cases of the diathermy group. Previously mentioned, and decreasing the number of hospital days in the expectant treatment group, was the fact that a number of cases were admitted as recurrent but quiescent, practically ready for operation.

There was no mortality in either group, whether treated expectantly, in combination with diathermy, or surgically.

#### SUMMARY AND CONCLUSIONS

The comparative study of these series of cases shows little to choose from in the light of percentage results. Statistics, especially in a limited group of cases are by no means conclusive, and we do not feel that they fully express the merits of diathermy applications in properly selected cases. The factors influencing the variation in hospital days have been discussed at length.

We believe that whatever good diathermy accomplishes is due to the increase in circulation brought about by the local application of heat, rather than from any heat generated in the diseased tissues themselves, and surely not from any destruction of bacteria by heat.

We do not agree with some observers that it should be employed in all cases of inflammatory disease irrespective of the severity of the infection and the degree of pelvic pathology.

Certain indications and contraindications must be borne in mind in the selection of cases; then no untoward results may be feared. Furthermore, it must be clearly understood that its use should be in conjunction with other recognized methods of treatment. It is neither to be relied upon alone, or regarded as a specific measure, and an accurate diagnosis by a gynecologist should precede its use.

It is best employed to advantage in young women experiencing their first attack, with or without adnexal masses, and in whom the acute symptoms and fever have subsided. It is of much less value in recurrent cases, and our feeling is that such patients should generally be operated upon. When a diathermy application in a selected case results in a marked "reaction," evidenced by severe pain and increased temperature, its use should be discontinued, for an indefinite period at least. It should never be used in the presence of fever, or when signs and symptoms of pelvic peritonitis are present.

Inflammatory cases of postabortal or puerperal origin apparently respond more advantageously than those of the neisserian group. Perhaps this is because the natural tendency of the former type of infection is to subside without permanent anatomic change.

Its use is contraindicated in the presence of complicating pelvic conditions as myoma uteri and ovarian cysts or tumors; neither should it be employed during menstruation or in the presence of profuse bleeding of inflammatory origin.

We did not find, as did some observers, that pain was almost instantly relieved by its use. Sometimes it was increased, for a time at least, and if markedly so, the applications were discontinued.

Less technical difficulty was noted, however, in the operative cases preceded by diathermy, as evidenced by decreased density of adhesions, and their more ready separation.

We were better satisfied with the use of the abdominosacral method than with the abdominovaginal, the application being simpler, and because of our belief that increased circulation is the principal factor in the benefit derived, rather than increased temperature in the tissues themselves which one might more likely expect a vaginal electrode to produce.

Whether longer or more frequent applications would increase the beneficial results is open to further investigation. Thus far, our facilities have not permitted this trial.

Bearing in mind these conclusions, our thought, after an unprejudiced study of this limited number of cases during the past year, is that diathermy is a helpful adjunct in the treatment of pelvic inflammatory disease, in properly selected cases.

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## A STUDY OF FIFTY CONSECUTIVE ECTOPIC PREGNANCIES\*

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ECTOPIC pregnancy has been a difficult condition to recognize ever since such pathology has been known to exist. The literature has not revealed any one test or symptom which will alone make the diagnosis certain. It was with this in mind that a study of the records of 50 consecutive ectopic pregnancies was made. The period during which these women came into the Evanston Hospital extends from January 1, 1922, to July 1, 1928. They were cared for on the service of Dr. William C. Danforth. We hope from this study to obtain a clearer knowledge of the significance of the symptoms, physical signs, and laboratory findings, and determine what method of treatment is most satisfactory.

There were many irrelevant symptoms given in these records. A small number occurred so regularly that we consider them of great diagnostic value. Of these, irregular bleeding and sudden lower abdominal pain were the two most frequent complaints being present in 89 per cent and 87 per cent respectively. Another very common symptom and one which should always make one suspect the condition, is amenorrhea, present in 73.5 per cent. The latter was not of any certain duration as is evidenced by the number of days from the last menses to the onset of symptoms. Fifty-eight per cent had no menstruation for from twenty-nine to seventy-four days. Forty-two per cent stated that their last period was less than twenty-eight days past. However it is probable that in many of the latter group, the last bleeding was not a normal flow but an irregular bleeding due to the ectopic pregnancy.

Symptoms of syncope were present in 53 per cent, such as fainting, pallor, and an increased pulse rate. Nausea and vomiting were frequent, but may be confusing, as they are present in other acute abdominal conditions. These were found in 43 per cent of our cases. It was interesting that so few cases actually showed evidence of shock, as it was found in only 11 per cent. Shoulder pain, which is a reflex sign of subdiaphragmatic pressure due to the free blood in the abdomen, was only found in 11 per cent. Bluish discoloration about the umbilicus, or Cullen's sign, was seen in but one instance.

Among physical signs, tenderness of the lower abdomen was found in 86 per cent. It was localized in one side in 69 per cent. Fifty-eight per cent had generalized abdominal rigidity or it was confined to one

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side. A palpable mass was found by abdominal palpation or bimanual examination in 52 per cent. The temperature was recorded in 42 of the 50 cases. Twenty per cent of these had a fever of one or more degrees. This was 10 per cent of the total cases and may have been due to an associated pelvic inflammatory process. The latter was found in nearly that percentage at operation. The pulse was under 100 in 55 per cent and between 100 and 120 in 36 per cent. The remainder or 9 per cent were over 120 and this latter number corresponds closely with the 11 per cent in which shock was present.

TABLE I. FREQUENCY OF SYMPTOMS

Irregular bleeding	88.8 per cent
Sudden pain	87.0 "
Amenorrhea	73.5 "
Syncope	53.5 "
Nausea and vomiting	43.0 "
Shock	11.0 "
Shoulder pain	11.6 "
Cullen's sign	2.0 "

TABLE II. FREQUENCY OF PHYSICAL FINDINGS

Tenderness	85.7 per cent
Not localized	31%
Localized	69%
Rigidity	57.5 "
Palpable mass	52.2 "
Fever	20.8 "
Pulse rate over 100	44.8 "
Breast changes	12.0 "
Pallor	16.0 "

The leucocyte count has been the most valuable laboratory finding. The hemoglobin readings were not as low as the pallor of the patient would indicate. The latter was made on 26 of our women and of these a reading of 70 per cent or above was found in eight instances. In 16 of these, the readings were between 50 per cent and 70 per cent. In one instance it was 40 per cent and in another 27 per cent. The hemoglobin reading does not greatly clarify the diagnosis, but sometimes transfusion is necessary and in these cases, it assists in determining when this is indicated. The leucocyte count was of more value in diagnosis, in that, a high count was found indicative of free blood in the peritoneal cavity. This did not necessarily mean a great deal of free blood, as it is present also with a moderate amount. There may be a high leucocyte count, then, long before a decided drop would be noticed in the hemoglobin test and the red cell count. The white blood cell count was made on 34 of our women. In 23 per cent the count was below ten thousand. There were 38 per cent between ten and fifteen thousand and the remaining 39 per cent were over fifteen thousand. Therefore in over three-fourths of the cases a count of over ten

thousand was found. We believe that the presence of free blood in the peritoneal cavity can be more quickly determined by a high leucocyte count, than by other signs.

TABLE III. LABORATORY FINDINGS

HEMOGLOBIN READINGS TESTED IN 26 CASES		LEUCOCYTE COUNT TESTED IN 34 CASES		
90-100	2	5-10 thousand	8	23.5%
80- 89	1	10-15 "	13	76.5%
70- 79	5	15-20 "	8	"
60- 69	10	20-25 "	4	"
50- 59	6	Over 25 "	1	"
40- 49	1			
27	1			

No one finding is sufficient to diagnose ectopic pregnancy. It is necessary to have a thorough knowledge of the symptoms, physical signs and laboratory examinations. Of the latter the leucocyte count is the most reliable and informative test. Posterior colpotomy was carried out in only a few of our cases. It was not deemed necessary as a routine method.

The associated pathology as discovered at operation and confirmed by the reports of the Pathologic Department of the Evanston Hospital, showed that salpingitis was present in 10.6 per cent. This is not as high as some other writers have reported. Ovarian cysts or parovarian cysts were found in ten cases, or 20 per cent. Fibroid tumors of the uterus occurred three times. As to the location of pregnancies in the tubes, it was found at operation, that one-half were in the left and the other half in the right tube. Eighty-two per cent were ruptured and only 18 per cent not ruptured. Of the former, 56.3 per cent were in the distal third of the tube, 12.5 per cent in the middle third, and 28.1 per cent in the proximal third. If the tube was not ruptured the ratio was reversed. The greater number or 50 per cent were in the proximal third, and 16.6 per cent in the middle third, and 33.3 per cent in the distal third.

TABLE IV. OPERATIVE FINDINGS: 50 CASES

25 IN LEFT TUBE LOCATION OF PREGNANCY IN TUBE	25 IN RIGHT TUBE	
	RUPTURED 82 PER CENT	NOT RUPTURED 18 PER CENT
Proximal third	28.1 per cent	50.0 per cent
Middle "	12.5 "	16.6 "
Distal "	56.3 "	33.3 "

In all but one instance operation was the method of choice as soon as the diagnosis was made. In this one, expectancy was followed for some time. A leucocyte count was taken for many days and at first several were taken daily. There was a variation from 14,800 to 9000, with a later rise to 10,000 over a period of eighteen days. A pelvic

inflammatory mass was suspected at first. But when operation was finally done a ruptured ectopic pregnancy was found as well as a pelvic infection. The fetus was 15.5 cm. in length. A great deal of difficulty was experienced in removing the mass and a large raw surface was denuded. In reviewing this case later it seemed that immediate operation would have been wiser, though the woman did make an uneventful recovery. This case has been cited to emphasize our contention that immediate operation is the best treatment. In the opinion of most writers it would appear this is the procedure of choice. Our usual procedure is as follows: The abdomen is quickly opened. The presence of free blood at once confirms the diagnosis. The offending tube is located as quickly as possible. If so much blood is present that the pelvic structures are obscured, the pregnant tube is rapidly located by the palpating fingers. The tube is brought into view and a clamp placed on the uterine end and another just outside the fimbriated end. If the condition of the woman permits and if the ovary is healthy, the tube is excised leaving the ovary in situ. Bleeding points on the anterior edge of the broad ligament are caught separately and ligated, after which the upper edge of the broad ligament is sewed over with a fine catgut suture. A wedge of tissue from the uterine horn is included with the proximal end of the tube to obviate the danger of a later ectopic pregnancy in the tubal stump. Should the condition of the patient be bad the tube and ovary are removed controlling hemorrhage by a figure-of-eight suture ligature taking in the entire upper portion of the broad ligament.

The opposite tube is not disturbed unless it shows sufficient changes to justify it. Other than removing large firm clots which are easily accessible, the removal of blood adds to the length of the operation and operative trauma. In none of our cases have we had reason to regret this course and it is possible that reabsorption of the blood may be of some value. We have only rarely found it necessary to use laparotomy pads. Intraabdominal manipulation should be minimized to the greatest possible degree. Postoperative care is simple. For the first twenty-four hours morphine sulphate is used rather freely and fluids are given as much as possible. Transfusion should be used in women who are greatly exsanguinated, but not until hemorrhage has been controlled.

In studying the length of time from the onset of symptoms to the day of operation it was interesting to note that trouble had been present before it was recognized. In many cases the symptoms were so slight that the patients did not consider their condition serious enough to call a physician. Many times when the early symptoms were merely irregular bleeding, not associated with severe pain, even though the patient had missed a period she would not be alarmed. Usually the sudden onset of severe pain is the first thing which leads her to call

the physician. When there has been no amenorrhea or irregular bleeding but only a sharp sudden pain, the white blood count was of great value. As Farrar points out, the white blood cell count is more marked during the first few hours after the occurrence of bleeding.

The mortality in our series was only 2 per cent. One woman died who was brought into the hospital in a critical condition, operated upon immediately, and died a little more than one hour after the operation.

No important information was gained from studying the ages or parity in these women. About 20 per cent were in the third decade of life, 60 per cent in the fourth, and 20 per cent in the fifth. This is about the same ratio as is observed among the women delivered of full-term babies. About 33 per cent were primiparae and 66 per cent multiparae. This also corresponds with the parities in full-term deliveries. In other words the incidence of ectopic pregnancies is similar to that period of a woman's life when she is most apt to be pregnant.

TABLE V. GENERAL DATA

Ages—		Para—	
Under 20 years	0.0 per cent	Primiparae	33.3 per cent
20-29 “	22.7 “	Multiparae	66.6 “
30-39 “	65.9 “		
40-45 “	11.3 “		
Number of Days From Last Period to Onset of Symptoms			
0-28 days	42.4 per cent		
29-74 “	57.6 “		

In conclusion therefore we believe that age and parity are of no help in the diagnosis of ectopic pregnancy. One must have the entire picture in mind, including the symptoms, physical signs, and laboratory findings. Of the symptoms, irregular bleeding, sudden onset of pain, and amenorrhea are the most important. Of the physical signs, tenderness and rigidity in the lower abdomen and a palpable mass, are most frequently found. In the laboratory findings the high leucocyte count is most valuable. It speaks strongly for recent bleeding into the peritoneal cavity when the count is 15,000 or over. With regard to treatment, operation was done as soon as the diagnosis was made. The abdomen was opened quickly, the pregnant tube found, and a simple salpingectomy done with as little trauma as possible.

(For discussion, see page 286.)

# PUERPERAL MORBIDITY WITHOUT DISINFECTION OF THE VAGINA\*

## AN ANALYSIS OF 2016 CASES

BY CHARLES A. GORDON, M.D., F.A.C.S., BROOKLYN, N. Y.

FOR some years, at St. Catherine's and Greenpoint Hospitals, we have managed parturition with, I think, consistent conservatism. Both hospitals receive ambulance cases, and all deliveries of service cases are conducted by interns, with staff supervision for abnormal cases.

Three years ago I analyzed 6562 consecutive cases of labor conservatively managed at both institutions; incidence and mortality of obstetric emergencies and operations were studied in an effort to show that low mortality depended largely upon minimum interference.

We have not interfered with what seemed to us would result in spontaneous delivery, and have terminated only difficult or prolonged labors. Over 90 per cent of our patients have no vaginal examinations at all. We are thoroughly satisfied with rectal examinations, but patients frankly progressing do without that. We are very slow to examine primiparae vaginally, but quickly examine multiparae who fail to progress. Morphine is freely used in the first stage of labor, and pituitrin not until completion of the third stage. Manual removal of the placenta is not done except for hemorrhage. The cervix is not routinely inspected, coincident operations are not done, and disinfection of the vagina is not practiced.

In mortality much is unavoidable. Trauma and hemorrhage we will always have. And possibly infection too. Morbidity, however, should be largely preventable, and all morbidity must be called puerperal infection, unless there is convincing proof of a lesion outside the generative tract, and absence of pelvic pathology as well. A vast amount of work has been done in an effort to determine its exact etiology, and progress is being slowly made. In the meantime, I feel sure that repeated study of results in our own cases will do more than anything else to teach us and those associated with us the importance of conservative obstetrics.

We were much impressed by the careful work of H. W. Mayes at the Methodist-Episcopal Hospital who has advocated intravaginal and intrauterine use of mercurochrome in labor. His figures were convincing, so good that he has suggested that its use before all vaginal examinations or instrumentation be made compulsory by law on the

\*Read at a meeting of the Brooklyn Gynecological Society, April 5, 1929.



same basis as the preventive treatment of ophthalmia neonatorum. "Vaginal examinations," he says, "should be the rule as they assist in getting the solution in contact with the entire mucosa."

Before beginning its use, however, we thought it best to evaluate our own experience with a simpler, perhaps more perfunctory method of preparation which consists of shaving the vulva, abdomen, and inside of the thighs and washing that area with soap and water. In St. Catherine's, one coat of 3.5 per cent iodine is applied just before delivery, while in Greenpoint another application is made at the time of preparation.

Not long ago David Kuperstein analyzed 1012 consecutive cases of labor, which occurred at Greenpoint Hospital during 1926 and 1927 in my service and the service of T. S. Welton. These cases are repeated here.

Various ideas for a study of morbidity have been proposed. The standards of the American College of Surgeons, Johns Hopkins, and the Congress on Puerperal Infection at Strassburg (1923) are about the same, while that of the British Medical Association and J. B. DeLee are much more rigid. For our study we selected the commonly used standard which was also chosen by H. W. Mayes and H. Bailey, in their work on mercurochrome in which we were especially interested, i.e., "A temperature of  $100.4^{\circ}$  on two successive days following delivery, not including the day of delivery and not occurring later than the tenth day."

Approximately 1000 consecutive cases from each institution were studied, the tabulation being done by David Kuperstein and Alfred W. Schenone to whom I owe warm thanks for the preparation of this material. In each instance the cases included only the cases occurring just prior to the time of the study.

Both hospitals maintain ambulances, and have a constantly changing intern staff, by whom all deliveries were done, with staff supervision for abnormal cases only.

In 1012 cases, including 10 cesareans at Greenpoint, there were 3 deaths, or 0.3 per cent mortality and 36 cases of morbidity, or 3.6 per cent. In St. Catherine's in 1004 deliveries there were 4 deaths or 0.4 per cent mortality with 37 cases of morbidity, or 3.7 per cent. The morbidity for 2016 cases was 3.6 per cent.

The similarity of these figures invited further analysis. A striking parallel is apparent in Table I which shows the character of the material.

No further details are presented because analysis of the methods of delivery shows a sufficient number of obstetric operations to indicate the varied nature of the material.

In classifying puerperal morbidity it is difficult to assign cases to any particular group with absolute certainty. The diagnosis of parametritis, common and simple as it is, often does not rest upon positive

proof; and so with lochimetra, and other lesions within the uterus. Table II indicates the causes found for the febrile reaction in our morbid patients, 73 in 2016 cases. If the number of cases in which the lesion was undetermined seems large, that is our common experience.

TABLE I. PRESENTATIONS AND POSITIONS

	ST. CATHERINE'S		GREENPOINT	
Vertex		957		958
Anterior	918		869	
Posterior	35		84	
Face	4		6	
Breech		44		51
Transverse		3		3
		<u>1004</u>		<u>1012</u>

TABLE II. COMPLICATIONS

	ST. CATHERINE'S	GREENPOINT
Parametritis	9	10
Lochimetra	7	4
Acute bronchitis	1	3
Pneumonia	—	3
Acute endocarditis	—	1
Nephritis	—	1
Phlebitis	2	1
Wound infection	8 (1 ABD.)	1
Influenza	2	—
Breasts	2	—
Pyelitis	1	2
Undetermined	5	10
	<u>37</u>	<u>36</u>

The essential point in such a study would seem to be the relationship of morbidity to the method of delivery. No deductions have been made in Table III for any reason. Nor should morbidity tables be corrected. The standard used should be rigid or it fails in its purpose.

There were 3 cases of manual removal of the placenta, in which other operative procedures were done; all showed morbidity. The number of spontaneous deliveries is high; over 92 per cent of all the

TABLE III. MORBIDITY CLASSIFIED AS TO METHOD OF DELIVERY

	ST. CATHERINE'S		GREENPOINT		TOTAL PER CENT MORBID
	TOTAL CASES	CASES MORBID	TOTAL CASES	CASES MORBID	
Spontaneous*	914	25	945	23	2.6
Forceps (low)	43	5	39	4	11.0
Forceps (median)	18	3	—	—	16.7
Breech extraction	10	—	8	4	22.0
Version	6	—	9	1	6.7
Bag induction	9	1	1	—	10.0
Cesarean section	2	2	10	4	50.0
Craniotomy	2	1	—	—	50.0
		Morbidity 3.6%			

\*Includes Breech.

cases studied, and their morbidity is low. That is significant, yet it is a not uncommon experience to see severe and fatal infection follow spontaneous delivery, while many cases of complicated delivery got well without incident.

The problem is a complicated one with many factors concerned in its ultimate etiology. Reduced to the simplest terms, infection and resistance are of the greatest importance. There is no doubt that exhaustion from long or otherwise difficult labor, with laceration of the cervix or perineum, are predisposing factors. Hemorrhage is so important that one can reasonably predict a febrile puerperium, if blood loss has been excessive. Possibly susceptibility to infection can be measured in terms of blood loss plus interference. At any rate, the length of the lying-in period depends largely upon these factors.

The average hospital stay in Greenpoint is fourteen days; in St. Catherine's eleven. In the 37 cases of morbidity at St. Catherine's the longest stay was forty-two days, and the average fourteen days.

#### MORTALITY

Though not directly concerned with mortality in this paper, the cases which died are briefly summarized as further indicating the nature of the material, 7 cases in all: (1) toxemia of pregnancy, spontaneous delivery, severe postpartum convulsion, died thirty-three hours after delivery. (2) Placenta previa marginalis, Voorhees' bag, spontaneous stillbirth, died of pulmonary embolism five days later. (3) Vertex in funnel pelvis, attempted forceps delivery at home, low cesarean section, died of shock and postpartum hemorrhage. (4) Breech, attempt at forceps delivery version and extraction, died of metritis and general peritonitis two days after delivery. The remaining three deaths occurred at Greenpoint; (5) cardiac decompensation one day postpartum, (6) rupture of the uterus following breech extraction, died twelve hours postpartum, and (7) the last died of lobar pneumonia seven days after delivery.

Infection may occur from within or without. Attempts to sterilize the birth canal are based upon the premise that reduction in the number of microorganisms present will minimize the risk no matter what else is done. This may be sound, but it is at least doubtful.

A tremendous amount of research has been done upon the bacterial content of the birth canal. That many microorganisms are normally present in the vagina, we know. When they appear in the uterus has not been definitely settled, although Harris and Brown have demonstrated them, with streptococcus predominating, in the lower uterine segment after labor has lasted six hours. Many of their cases, however, with streptococcus in the uterus have not been seriously ill, and in their recent fine bacteriologic study of 113 cases of streptococcus puerperal infection, they produce evidence to show that aerobic beta

hemolytic streptococci, which are generally admitted to be the most serious invading organisms, were almost invariably introduced from the outside at the time of labor or early in the puerperium. This would seem to be an excellent argument for conservatism, yet A. B. Davis says that for thirty-seven years, in 80,000 cases at the New York Lying-In Hospital, they have yet to see bad results from vaginal examinations required every two hours in the out-patient clinic before delivery.

That most organisms are saprophytic and nonpathogenic is probable. That these same bacteria may assume other characteristics is possible. That their wholesale destruction is beneficial is doubtful. Tissue damage may result in disturbance of the natural cellular defense mechanism of the vaginal secretions, parametrium, uterine wall, and the entire reticuloendothelial system. Many chemicals have been used. Let us look at the most popular, mercurochrome.

H. W. Mayes reported 300 cases delivered with his mercurochrome technique, with a morbidity of 12.6 per cent, and collected enough figures from other Brooklyn hospitals to increase the number to 2,299 cases, with a morbidity of 6.8 per cent. Two and a half years of routine delivery with mercurochrome at the Methodist-Episcopal Hospital showed 3,500 cases with a morbidity of 8.6 per cent; cesareans were not included, I believe. A morbidity of 29 per cent in 93 bag cases was reduced to 11.5 per cent in 78 bag cases with mercurochrome technique.

Bourne quotes 582 consecutive cases of induction by bougies or bags at the Queen Charlotte Hospital, with a morbidity rate of 15 per cent and only one death from sepsis. He thinks that induction of labor is a remarkably safe operation although there is an increased risk of mild sepsis, serious infection being seldom seen.

Simmons states that 2 per cent alcohol acetone aqueous, and 5 per cent alcoholic mercurochrome are comparatively feebly bactericidal, and that 3.5 per cent iodine is far superior. Rodriguez, in his work on disinfection of the mucous membrane of the mouth, says that 5 per cent alcoholic mercurochrome, and mercurochrome alcohol acetone preparations possess decided advantage over aqueous solutions, but they fail in too large a proportion of cases to be considered effective, and that 3.5 per cent iodine or even 1.75 per cent preferably in glycerin is an effective germicide. Reddish and Drake feebly defend mercurochrome, which they found as good as iodine, not better, but preferable on account of the well-known objections to iodine. Scott and Hill advocate 2 per cent alcohol acetone mercurochrome as an effective germicide for skin disinfection. Tinker and Sutton conclude that iodine and mercurochrome are both inefficient.

#### SUMMARY

We have presented 2016 average cases of labor, with a morbidity of but 3.6 per cent. These patients were delivered by interns with but our routine preparation of the outside field, and without any attempt to disinfect the vagina. For our iodine we hold no brief, but I believe that conservative obstetrics, with minimal interference, is the best protection against puerperal infection. Our series is small; possibly more figures would increase our morbid rate, perhaps not. I feel sure that somewhere lies the irreducible minimum. The whole question of

vaginal antisepsis is still an open one. Although excellent results have been unquestionably obtained, coincident with the use of mercurochrome, there is grave doubt of its value as a sterilizing agent. The widespread use might give a false sense of security to those whose obstetric judgment is outdistanced by their desire for rapid delivery.

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(For discussion, see page 293.)

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## TREATMENT OF ENDOCERVICITIS WITH ACTUAL CAUTERY AND ELECTROCOAGULATION\*

BY WALTER F. HARRIMAN, M.D., PHILADELPHIA, PA.

(Clinical Instructor in Surgery, Temple University and Associate Obstetrician, Kensington Hospital for Women)

THE incidence of endocervicitis in multiparous women has been variously estimated at from 25 to 35 per cent. From the time of Emil J. Noeggarath we have known that many of these cases were of gonococcal origin. Perhaps an equal number are the result of trauma. How many times the obstetrician finds a latent disease of the cervix on postnatal examination! Trauma, no matter how minute, exists even after normal delivery, and the increasing frequency of instrumental and manual interference raises the incidence of endocervicitis.

From the standpoint of treatment we class endocervicitis as acute and chronic. The acute condition as seen in an office practice is almost never due to trauma but is of an acute infectious origin. Its treatment is wholly medical.

In seeking the most efficient method of curing chronic endocervicitis, we may group the various means of destroying tissue under the following headings: (1) Excision; (2) chemical destruction; (3) heat destruction, (a) actual cautery, (b) diathermy; (4) electrical fulguration, desiccation and coagulation.

\*Read before the Obstetrical Society of Philadelphia, Stated Meeting, January 3, 1929.

Excision, or amputation, of the cervix is a major operation. Often the infected area is not entirely removed and the old erosion returns. Sterility, abortion, and early miscarriage have been ascribed to it.

Chemical applications of acids, alkalies, or strong astringents might prove of value were it not for the following factors: (1) The extent of their action is indefinite. (2) The area of application is difficult to control. (3) Healing following their application is notoriously slow and produces deep scarring.

The actual cautery has been and still is one useful method of curing endocervicitis. The cautery point itself must of necessity be small enough to enter the external os. If the cautery is too hot, the opera-

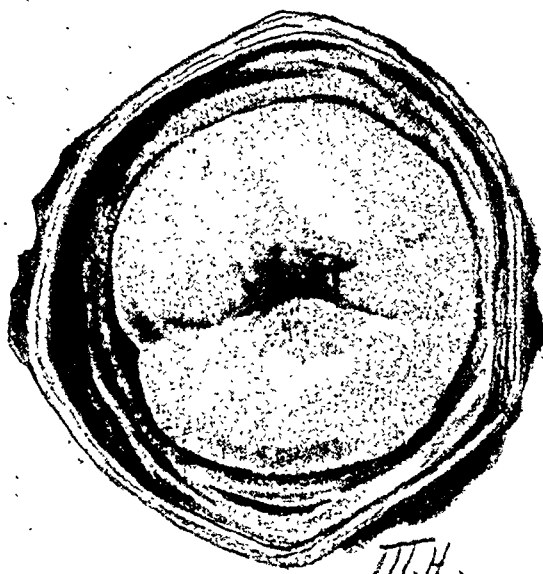


Fig. 1.—Multiparous cervix showing moderate erosion.

tion is followed by bleeding, yet in certain extensive lesions a destructive heat must reach deeply into the cervical substance. After using various forms of cautery points, we believe a small nasal cautery with a controlling rheostat to be most efficient. In moderate cases of endocervicitis with only a slight increase in size of the cervix and with little or no cystic degeneration, a stripping of the canal and lips of the cervix assures a cure. In those cases of old standing where the cervix is inflamed, three or four times its normal size, and contains numerous nabothian cysts, electrocoagulation (which will be described later) is far superior.

In our hands, diathermy, as a method of treating endocervicitis, has failed. This method of treatment is based upon the well-known fact that the gonococcus has a low thermal death point. By inserting a

small electrode into the cervical canal, or around the cervix itself, and passing through it a high frequency current, it has been well proved that the electrode may be heated to  $118^{\circ}$  F. as measured by a thermometer inserted within the electrode itself. We have been able to raise the temperature within the electrode to  $118^{\circ}$  F. as has been advocated and this heat has been sustained for various periods of time, yet even after three or four applications the cervix has remained infected, the erosion only partially cured, and the nabothian cysts unaltered. The cause for failure by this method we believe to be due to the following reasons:

1. Not all cases of endocervicitis are of gonococcal origin.
2. In advanced cases with cystic degeneration the degree of heat is not sufficient to affect the nabothian cysts. They must be destroyed.

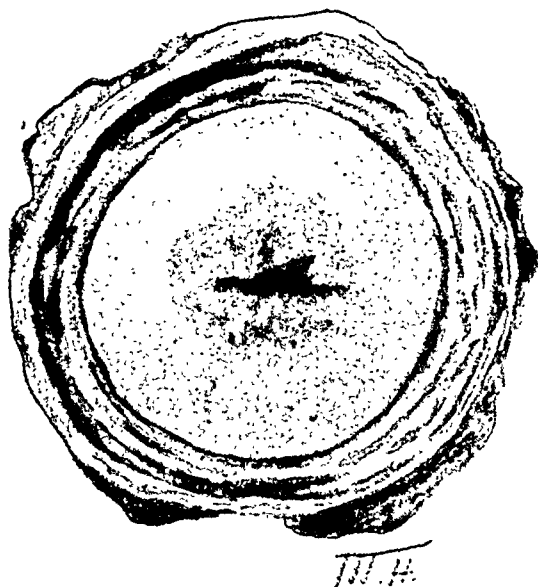


Fig. 2.—Extensive erosion with involvement of the cervical canal.

3. All old cases of endocervicitis, no matter what their original etiology, become a mixed infection, and many bacteria have a higher thermal death point than may be safely obtained by this method.

4. The cervix has a rich blood supply and although the surface of the electrode may reach a temperature of  $118^{\circ}$  F. the circulating blood and lymph rapidly dissipate the heat, so that even  $\frac{1}{4}$  inch from the electrode the temperature is much less than  $118^{\circ}$  F. and in certain cases of endocervicitis the pathology extends  $\frac{1}{2}$  inch, or more, into the cervical tissue.

After treating some two hundred odd cases of endocervicitis by the actual cautery and electrocoagulation method, we have been impressed with the striking success of electrocoagulation. It is by far the quicker method, and we have yet to fail in a *permanent cure*. Healing

is more rapid, scarring is lessened, and we have never had a single case of bleeding following its use.

The technical application of the current has never been well described. Articles on the subject leave one with a hazy idea of its use in the cervix and do not accurately describe the technic in lesions of different extent. Unfortunately machines now on the market are not made to a single standard. The variation in current supplied differs markedly. Milliampere readings vary from 200 to 2500 and give no index as to the depth of tissue destruction, which depends upon the size of the electrode, the conductivity of the tissue, and resistance, or thickness, between the active and indifferent electrode. We have devised the following test which quite accurately assures one of the proper adjustment of current. A piece of liver, or, fresh veal, one inch

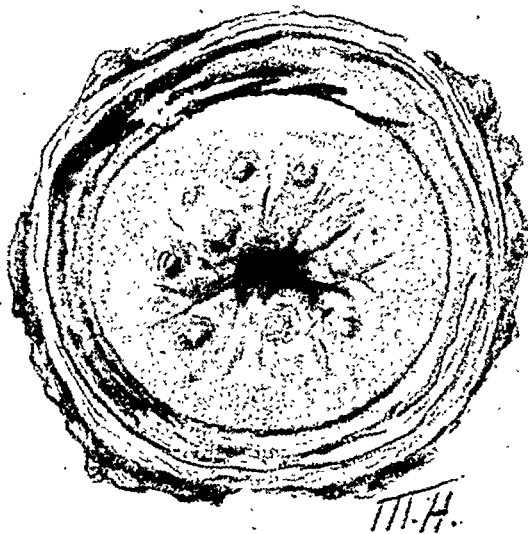


Fig. 3.—Final stage of endocervicitis showing nabothian cysts deeply embedded in the cervical tissue.

in thickness and three or four inches square is placed upon the indifferent electrode. The active electrode which is pointed and about the size of a large darning needle and protected by a rubber tubing so that only one-fourth of an inch of the pointed tip is exposed, is thrust downward in the middle or center area of the tissue. The current is now turned on for a period of one second (the length of time required to articulate the figures 1001). On slitting the tissue to obtain a cross-section at the area of contact, the current should be adjusted so that the tissue immediately around the puncture is white and appears coagulated and the coagulated area should not extend beyond the portion of tissue actually in contact with the electrode. The lowest setting of the levers or dials that will produce this coagulated appearance in one second is noted and this test need not be repeated.



Obviously the actual extent of the lesion in the cervix varies greatly. One case shows only slight affection of the columnar epithelial lining of the cervical canal with a slight erosion. In another case the ducts and glands are invaded, the eroded area is large, and the lesion extends deeply into the cervix from the canal. Still another case presents a greatly enlarged cervix with surface and buried nabothian cysts. The treatment for the first case is insufficient for the second and third, and the amount of destruction necessary for the third case would be uncalled for in the first.

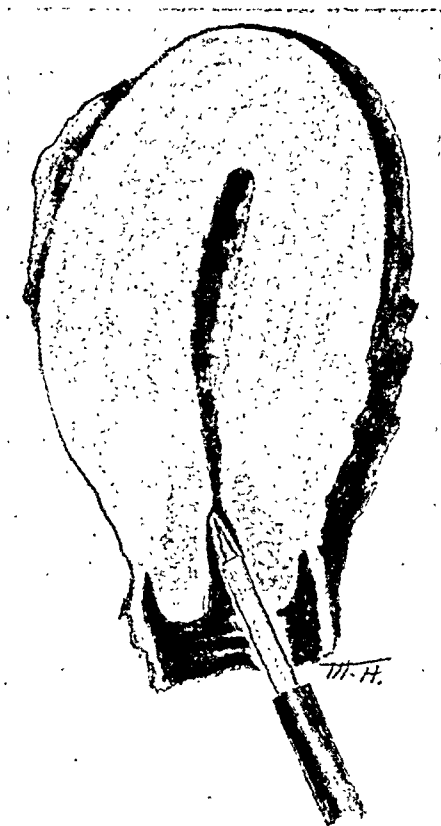


Fig. 4.—Position of electrode at start of stripping operation. The tip of the electrode is placed at the internal os.

Figs. 1, 2, and 3 represent three general types of endocervicitis. Most conditions found are variations or intergradations of these types.

Fig. 1 represents a superficial type of lesion. The erosion is slight, but on passing a sound, a sense of roughness is felt between the internal and external os, mucus streams from the canal, and a slight leucorrhea is always present. The active electrode, protected by a thin rubber tubing to within  $\frac{3}{8}$  of an inch of its tip, is passed into the canal as far as the internal os and pressure is made against one side of the cervix to make good contact (Fig. 4). The current is turned on with

the foot switch (a necessity for proper control of the current) for a few seconds while the electrode is slowly withdrawn to the external os, at which position the current is turned off. This process is repeated until four or five sections of the canal have been "striped," or, "cogwheeled." The tip of the electrode is now placed against various areas of the erosion while the current is turned rapidly on and off, or, "flashed." The eroded area will now have a whitish, coagulated appearance. It must be remembered that the heat and coagulation is in the tissue touched by the active electrode. Once the tissue in the immediate vicinity of the electrode has become coagulated a prolongation of the current tends to dry the coagulated area so thoroughly that arcing, or, sparking takes place as the current jumps from the elec-

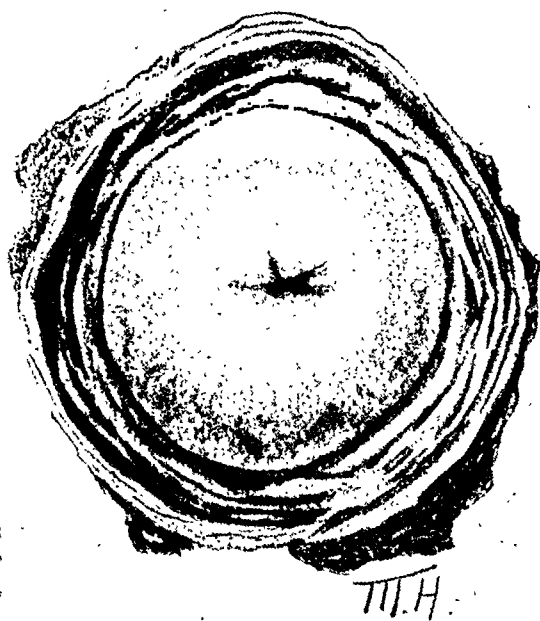


Fig. 5.—Same as Figs. 2 and 6. Showing the appearance after coagulation.

trode to more moist tissue beyond the coagulated area, however, it serves a purpose. Where the lesion is deeply seated and one desires the maximum effect, the current may be applied in one position until arcing begins and then the current again applied when the electrode is placed in a new position.

Fig. 2 illustrates a more extensive lesion which is treated as that of Fig. 1 with the exception of time of application. Here the electrode remains in contact with any certain area of the cervical canal for a longer period of time, the electrode drawn more slowly from internal to external os, just rapidly enough to prevent arcing. The erosion on the vaginal surface of the cervix is treated in the same manner as previously described, being certain that the entire area has become white in color which is proof of its coagulation.

Fig. 3 demonstrates the final stage of cystic degeneration. Here an application to the endocervical canal similar to that of Type 2 suffices and will destroy the deeply-seated cysts which often explode with an audible sound. The vaginal surface of the cervix, however, must be treated more drastically. The sharp point of the electrode is thrust into the cervix the depth of the exposed point, at a position equidistant between the external os and the circumference of the cervix. The current is now turned on with the foot switch until there is a tendency to arcing when the current is switched off and the electrode withdrawn. This is repeated until a ring of punctures has extended around the cervix.

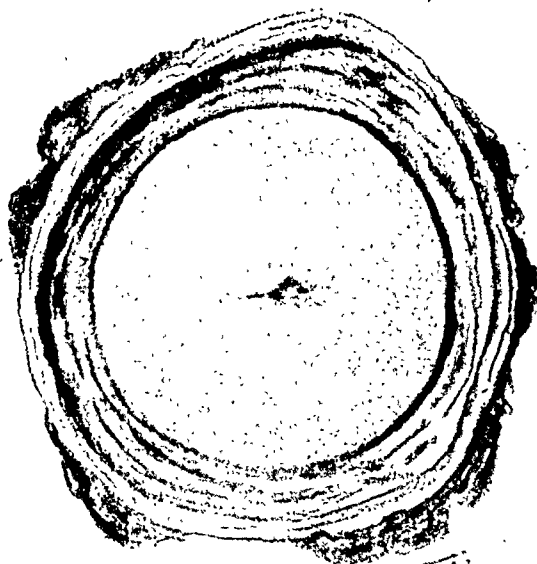


Fig. 6.—Same as Figs. 2 and 5. Cervix six weeks after coagulation.

In certain cases where a laceration of the cervix is present, one portion of the cervical lip may become thickened and hypertrophied. This hypertrophied lip may be reduced to normal size by a series of puncture applications along its axis.

The patient must be warned that her discharge will become more profuse for a period of two or three weeks. She reports to the office for weekly inspection and a daily douche of a mild antiseptic powder is ordered. After a period of three to five weeks, healing is complete. There is no pain following the electrocoagulation and a cure is certain.

Figs. 2, 5, and 6 represent the same cervix before treatment, immediately after coagulation, and the final result. The smoothness of the cervix, the decrease in size of the external os, and absence of visible scarring is not exaggerated.

## A CASE ILLUSTRATING THE VALUE OF THE X-RAY AS AN AID IN THE MANAGEMENT OF POLYHYDRAMNIOS\*

BY ALFRED C. BECK, BROOKLYN, N. Y.

THE usual treatment of polyhydramnios is expectant. A desire to obtain a viable child often leads us to postpone interference until pressure symptoms on the part of the mother become sufficiently grave

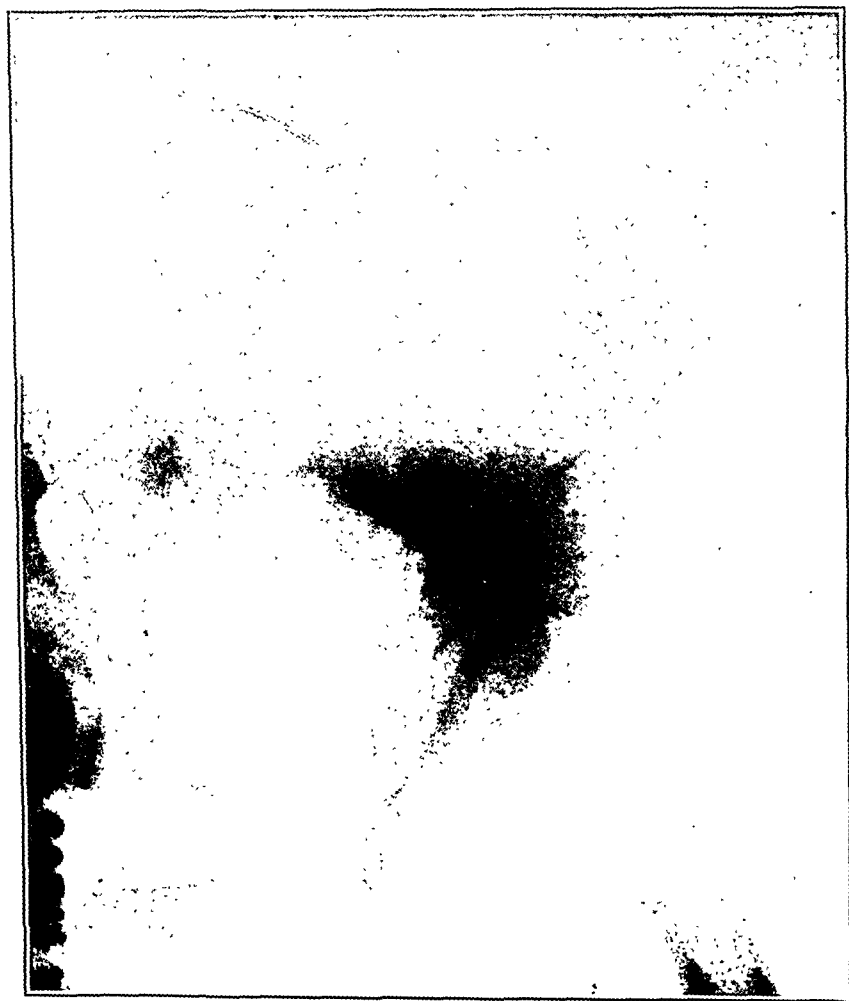


Fig. 1.

to warrant a disregard of the child's interests. After much discomfort and a not inconsiderable increase in the maternal risk, the pregnancy often terminates in the birth of a monster. The high incidence of fetal

\*Read at a meeting of the Brooklyn Gynecological Society, February, 1929.

anomalies in these cases should lead to a careful x-ray search for their presence. If a grave defect is discovered, the child may be disregarded and prompt rupture of the membranes will spare the mother much suffering and greatly diminish the risk.

The following case illustrates the value of an x-ray search for fetal anomaly in the management of polyhydramnios.

Mrs. B. D., aged twenty-seven, was referred to me September 27, 1928. She was then in the twentieth week of her third pregnancy. Both of her previous children were born at term and were perfectly developed. Her history and physical examination were quite normal. She was seen twice in the following two months and abdominal examinations showed the usual findings of an ordinary pregnancy. On the twenty-second of November (twenty-ninth week) the uterus was enlarged out of proportion to the period of gestation. This was definitely due to an excess of amniotic fluid and the fetal heart could not be heard. Two weeks later (thirty-first week) the fundus reached the ensiform and proportionate enlargement was observed in all directions. No fetal parts could be palpated. Within a few days the patient began to complain of pressure symptoms and was brought to the hospital. On admission, December 11, 1928, examination showed the uterus to be enormously distended, and an edema of the lower part of the abdominal wall and lower extremities. The patient complained of general abdominal discomfort, nausea, dyspnea, and insomnia, but refused to permit rupture of the membranes as she wished to have the pregnancy continue as long as she could bear it. The possibility of the presence of a monster was suggested to the husband and permission for an x-ray examination was granted. The x-ray showed the child to have a relatively small head. Believing the condition to be hemierania, immediate interruption of the pregnancy was recommended and accepted. The membranes were ruptured and about eight liters of amniotic fluid drained away. Labor began one hour later and resulted in the spontaneous delivery of a hemicephalic monster. Aside from slight difficulty in the third stage, the labor was quite normal. Convalescence was uneventful and the patient was discharged from the hospital at the end of two weeks.

#### CONCLUSIONS

1. By the aid of the x-ray in this case, a definite decision to empty the uterus was reached.

2. While the same conclusion no doubt would have been formed at a later date without the aid of the x-ray, the patient was spared considerable suffering.

3. Early interference, before the appearance of maternal indications for interruption of the pregnancy, greatly lessened the risk in polyhydramnios.

20 LIVINGSTON STREET.

## UTEROCYSTOGRAPHY\*

BY E. C. STEINHARTER, M.D., F.A.C.S., AND SAMUEL BROWN, M.D.,  
CINCINNATI, OHIO

THE favorable use of opaque mediums for uterine and tubal diagnosis has been reported by us,<sup>1, 2</sup> as well as by others. More recently, Robins<sup>3</sup> has called attention to another aid, namely, cystography, for diagnosing conditions affecting the female pelvis, but apparently the method has received less attention than it merits. Although we recognize the value of the procedure he advocates, it occurred to us that perhaps the use of uterography and cystography in combination would have advantages over either method used alone and since the spring of 1928, we



Fig. 1.—Radiograph after lipiodol injection into the uterus showing right tube occluded, left tube enlarged at distal end.

have been employing the two together in the gynecologic clinic. So far as we know, they have never been used simultaneously before. We submit the following uterographs to illustrate in a limited way their application.

This is a preliminary report, submitted in the hope that others will make use of the combined method of uterography and cystography and will publish their results.

The uterograms, Figs. 1, 2, and 3, illustrate the possibility of diagnosing adhesions between the uterus, fallopian tube, and urinary bladder, or an encroachment of any other adventitious structure upon the distended urinary bladder.

Our short series of cases leads us to conclude that the combined method has all the advantages of uterography alone and in addition,



Fig. 2.—Same as Fig. 1, after bladder had been filled with weak 10 per cent bromide solution. Operation showed that central concave depression of bladder was due to a subserous fibroid. Lateral depression was due to the fixed fallopian tube.



Fig. 3.—Radiograph showing V-shaped depression due to adhesions between uterus and bladder. In this case after first making a radiograph of the uterus, the uterine cannula was removed before filling the bladder, in consequence of which some of the oil drained out of the uterus, and this accounts for the incomplete uterine shadow. Adhesions were confirmed at operation.

by means of studying the contour of the distended bladder, it permits a visualization of the field beyond the reach of simple uterography, i.e., in the uterovesical space as well as in the areas lateral to the bladder.

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# A NEW UTERINE CANNULA, GAS-TIGHT, OIL-TIGHT, AND SELF-RETAINING

By SAMUEL R. MEAKER, M.D., F.A.C.S., BOSTON, MASS.

(Associate Professor of Gynecology, Boston University School of Medicine)

THE cannula most commonly used for insufflation of gas and injection of iodized oil into the uterus, carries on its shaft a rubber or metal "acorn," which fits into and plugs the os externum. This instrument has two disadvantages. First, it often fails to give perfect

FIG. 1

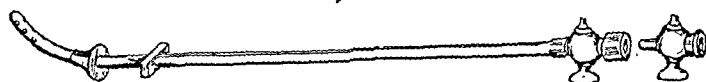


FIG. 2

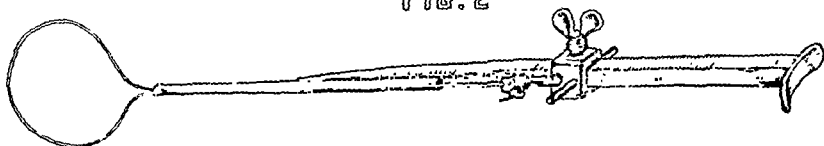
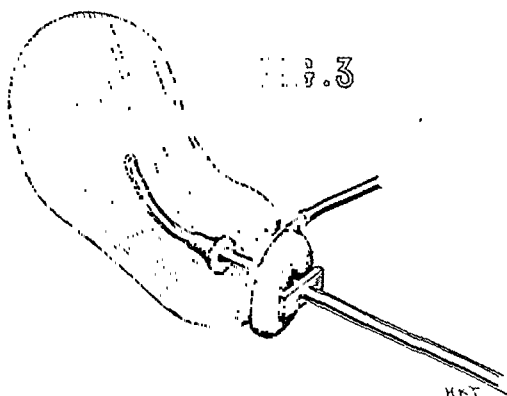


FIG. 3



obturation; in many cases, particularly when the cervix is lacerated or softened, a certain amount of regurgitation is unavoidable. Second, it requires constantly to be held in position, either by the hand of the operator or by an awkward assembly of volsella, ratchets, and screws.

The apparatus here presented\* works on a different principle. It comprises two instruments, the cannula proper and a light snare. The cannula has on its shaft, one inch from the tip, a bell-shaped rubber button, which fits entirely within the cervix and occupies the upper

\*Made by Codman and Schurtleff, Boston, Mass.



half of the endocervical cavity. The snare is equipped with a loop of soft iron wire, which is made to encircle the lower half of the cervix. As the loop is pulled tight, the endocervix is firmly pressed on all sides against the flaring edge of the rubber button; thus perfect obturation is obtained. At the same time the lower half of the cervical canal is so constricted that the escape of the button becomes impossible.

This apparatus offers the following advantages:

1. It gives gas-tight and oil-tight obturation in all cases. Test pressures up to 350 mm. of mercury have been used without causing regurgitation.

2. The cannula is self-retaining against any force except a strong direct outward pull. It will remain in place throughout an operation, or during such moving of the patient as may be necessary for purposes of x-ray.



Fig. 4.

3. The instrument is adapted to all cervices, irrespective of their size, shape, and consistency.

4. The use of this apparatus causes a minimum of discomfort to the patient. In most cases the os externum will admit the button, which corresponds in size to a No. 18 Hanks dilator, without preliminary dilatation and without counter-traction on the cervix. Constriction of the cervix by a wire loop is less painful than the usual application of a volsella.

5. The natural position of the uterus is not disturbed by unintentional pushing or pulling. The organ can, however, be moved by manipulation of the cannula, if an alteration in its position is desired.

6. With the cannula introduced and the snare applied, the vaginal speculum may be removed. Thus only two light instruments remain in the vagina during insufflation or injection, and x-ray pictures are not marred by the heavy shadow of the speculum.

7. A cross-bar, located on the shaft of the cannula  $2\frac{1}{4}$  inches from the tip, serves as a marker to indicate when the instrument has been introduced far enough, and as a guard to prevent it from penetrating too deeply.

8. The cannula itself is calibrated to take the nozzle of the standard Record syringe. By means of the adapter it may be connected with the standard Luer syringe, or with rubber tubing.

9. Two pet-cocks, one in the cannula and one in the adapter, allow the joint between delivering apparatus and cannula to be broken without leakage of oil either from the delivering apparatus or from the uterus.

475 COMMONWEALTH AVENUE.

## A CASE OF PREGNANCY IN UTERUS DIDELPHYS

BY H. M. MILLS, M.D., F.A.C.S., AND HYMAN STRAUSS, BROOKLYN, N. Y.

MRS. W. B., a negress of twenty-six, born in U. S., para iii, gravida 4, came to the Prenatal Clinic of the Kings County Hospital early in August, 1928, expecting to be delivered about the middle of the same month. Her general history was negative. Obstetrically, three previous labors all normal, with living children,



Fig. 1.

all being breech deliveries. All the pregnancies were in the right uterus. During her previous delivery at this hospital, April 14, 1927, she had a postpartum hemorrhage. Her next and last menstrual period was in November, 1927, on time and normal in all respects; which made the expected date August, 1928. Her general condition had been excellent with no complaints.

Examination showed a well-nourished and developed multiparous negress, with a slight thyroid enlargement.

Measurements were normal.

The vagina was divided by a subseptum at the introitus, which protruded from the vulva during pregnancy and was very edematous. The fact that part of the septum was located between the cervixes and part at the introitus and the raggedness of the edges leads one to believe that the septum was torn during previous labors. The left cervix was multiparous, slightly softened and had a suggestive bluish tinge; while the right cervix was parous, lacerated, extremely soft and very blue. The left uterus was retro- and sinistroverted, the size of a small grape fruit, while the right one was as one would expect in a normal uterus at term. Frankly,

if one did not suspect a double uterus from the two cervices, one might overlook the left one, because it was definitely overshadowed by the one on the right. The uteri were freely movable and independent of each other. The adnexa were not palpable. Three days later she entered the hospital in active labor with a frank breech presentation, position L.S.P., pains every twenty minutes, presenting part

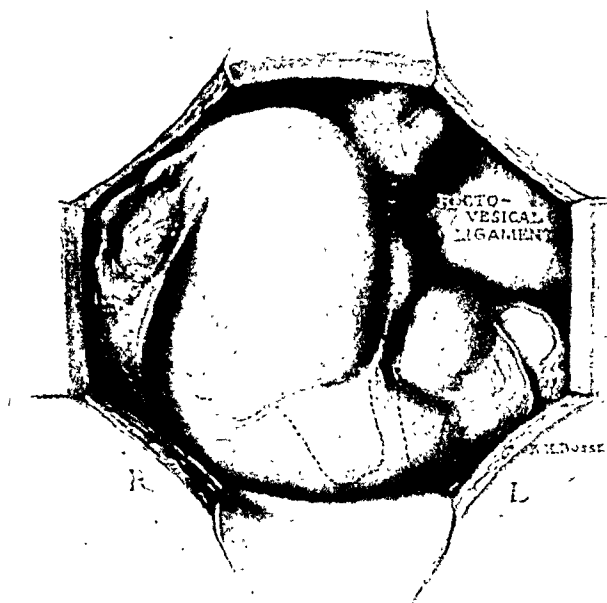


Fig. 2.



Fig. 3.

dipping in pelvis, membranes intact, cervix not effaced, two fingers dilated and fetal heart 140. Twenty hours later, under ether anesthesia, the frank breech was broken up, both feet brought down without difficulty, care being taken to avoid straddling the septum. The child, a female weighing 7 pounds, 12 ounces, was normal in every respect. There was no laceration and no postpartum complication except a mild cystitis which subsided in a few days. On discharge the findings

were essentially negative, the right uterus being normally involuted while the left one was now the size of an orange.

Five weeks postpartum, the patient came back complaining of severe pain on the right side for which a diagnosis of subacute appendicitis was made. Both she and her husband insisted that she be sterilized during the appendectomy. Laparotomy under ether anesthesia confirmed the diagnosis, the appendix was removed by the usual technic. The tubes were excised at the cornua, ligated, and buried. Examination of the internal genitalia showed two uteri separated by the rectovesical ligament at the level of the internal os of each uterus. The left uterus was slightly larger than the thumb, the right one was about three and one-half times as large. The right uterus was anterior in position, well involuted and freely movable, while the left one was in second degree retroversion, but otherwise normal in all respects. The ovary, tube, and round ligament on the left, were not so well developed. Further details are best shown in the diagram.

1133 FOSTER AVENUE.

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## REPORT OF A CASE OF TERATA KATADIDYMA

BY C. E. UPDEGRAFF, M.D., AKRON, OHIO

Mrs. A. E., aged twenty-four, white, para i, last menstruation June 30, 1928. Family and personal history negative; physical examination revealed an apparently normal individual. No history of multiple births in her own family or that of her husband as far as either knew. The first six months of pregnancy progressed normally, then uterus increased in size rapidly, an apparent typical hydramnios developing. A twin pregnancy could not be diagnosed, only one heart could be heard.

On Feb. 8, 1929, labor pains began about 1:00 A.M. and first stage progressed rapidly, the head being on the perineum at 6:00 A.M. Dilatation of the perineum was somewhat slow and median episiotomy was done at 9:00 A.M. followed shortly by delivery of the fetus. The membranes had ruptured at 5:00 A.M. with expulsion of a large amount of liquor amnii.

The fetus presented the typical picture of terata katadidyma, the fission being complete up to the umbilicus. There was one cord, four arms, one face, with two ears in the normal situation. The occiput was much broadened and in the center of the occiput were two ears close together.

### PATHOLOGIC REPORT

The specimen is a prosopothoracopagus. It consists of twin girls of about seven or eight months united above the umbilicus. The individual bodies are facing each other and bony fusion has occurred between the two thoraces and between the two frontal bones anteriorly and the two temporal bones posteriorly. There is a very broad, but otherwise well formed face anteriorly, and posteriorly the two ears, which do not enter into the formation of the face are situated about 0.5 cm. apart. The two anterior fontanelles are fused into a large triangular space. Thus each individual has well formed right and left ears, arms, and legs, and there are separate cervical and dorsal spines. There is a single umbilical cord.

There is a single esophagus. The stomach is single and somewhat butterfly-shaped, there being two cardiac pouches as if two stomachs were fused at the lesser curvature. There is a single well formed pylorus, and a single small intestine for a distance of about 22 inches at which point a well marked dilatation occurs.

In contact with this dilatation, but not communicating with it, is the blind proximal end of the small intestine of the left individual. Beyond this dilatation the intestine of the right individual continues in a normal manner.

There are two hearts, four lungs, two livers, two pancreases, two spleens, and four kidneys. The umbilical vessels communicate directly with the liver of the



Fig. 1.

left individual which is considerably larger than the liver of the right individual, which, however, possesses a fibrous connection with the umbilical vessels, but without evident circulatory connection.

For the pathologic report I am indebted to Dr. T. Harris Boughton, pathologist to the City Hospital of Akron.

SECOND NATIONAL BUILDING.

# SUPRAPUBIC TRANSVESICAL OPERATION FOR VESICOVAGINAL FISTULA

## REPORT OF TWO ADDITIONAL CASES

BY NATHAN P. SEARS, PH.D., M.D., SYRACUSE, N. Y.

*Assistant Professor of Gynecology at Syracuse University Medical College*

CLOSURE of a vesicovaginal fistula through a suprapubic incision into the bladder has been a much more popular procedure in Europe than in America. Recently, however, some interest in this operation has been evidenced by the appearance of reports of cases by C. A. Roeder and H. H. Young.

Following the report of Young's case, I had an opportunity to operate for a vesicovaginal fistula following hysterectomy. Since former experience had shown access to postoperative fistulas to be difficult per vaginam, this procedure seemed to give promise of better exposure. It was therefore tried with success and very soon thereafter another patient similarly afflicted was cured in the same manner.

In examining several American textbooks on gynecology, very little was found concerning this method of closure. Dudley,<sup>1</sup> Crossen,<sup>2</sup> Anspach,<sup>3</sup> Graves,<sup>4, 5</sup> and Bland<sup>6</sup> did not mention the suprapubic cystotomy incision for this condition. Kelly<sup>7</sup> describes a case operated upon by MacGill by this method, and Kelly and Burnam<sup>8</sup> suggest the operation, as first described by Trendelenburg, for inaccessible fistulas. Since the beginning of my study of this subject, Kelly<sup>9</sup> writing the chapter on "Urethra and Bladder" in his new book, states, "The transvesical route without opening the peritoneum at times affords an admirable access to a fistula which can be sewed up in situ by denuding and uniting its mucous margins." Ward<sup>10</sup> discussing the subject of vesicovaginal fistulas in Lewis' new system of surgery makes the following statement: "The suprapubic operation is more severe and has a greater mortality than the vaginal operation. In many cases it is impracticable owing to the fat abdominal walls."

In reviewing the literature, it was found that credit for devising this operation is universally given to Trendelenburg<sup>11</sup> who first performed it in 1880. He was able to cure only 1 case out of 3, in the other 2 finally resorting to colpocleisis.

Willi Meyer<sup>13</sup> was next to use this technic and failed in 2 cases. In 1 he made one attempt before performing colpocleisis and in the other case he made two attempts and finally gave up, again to use colpocleisis.

MacGill<sup>12</sup> was more successful although his first case can hardly be classed with this group since he did only a suprapubic drainage and the fistula closed itself. In his second case he opened the bladder and separated the vesical and vaginal walls at the margin of the fistula. He closed the bladder side of the fistula through this incision and then from the vaginal route closed the vaginal wall. Both cases were cured.

One of the first to review the reported cases was Louis Thiers.<sup>14</sup> He collected reports of 10 cases which gave the following results; 6 cures, 2 partial cures, and 2 failures. From his study he formed these conclusions: The indications for this

operation are; long narrow vagina, high fistulas, marked fixation, and unusual destruction of the vaginal wall. He went into some detail as to the supposed disadvantages, such as the formation of suprapubic sinus added to an uncured fistula, increased danger of abdominal operation, formation of stone and formation of hernia. Thiers felt such complications would be rare.

Dupin<sup>15</sup> gave a similar review but was more pessimistic as to the value of the operation. He classes as failures cases in which a urethral fistula, complicating the vesicovaginal fistula, failed to heal, and also cases developing vesical stone.

Dr. H. A. Kelly<sup>16</sup> in 1906 reviewed some important contributions to this subject. He emphasizes the following points: (1) plain catgut should be used for all sutures exposed to the bladder cavity, (2) the operation is often of value and of comparative simplicity and is best adapted to those fistulas following complete extirpation of the uterus, and (3) prolonged drainage and gentle irrigation with boric acid.

Everke,<sup>17</sup> operated upon three cases, the first in 1897. This first patient deserves special attention, having had three previous attempts, the first and second were efforts to close the fistula through the vagina, the third was colpoceleisis. Everke performed the Trendelenburg operation successfully and later reestablished the vaginal canal. The second case had had one vaginal attempt. The suprapubic operation closed the fistula, but a urethral fistula remained. In both of these cases Everke used silk sutures and stones formed. These later were removed. In the second patient the urethral fistula was subsequently closed from below. The third patient died. The operator, failing to place catheters in the ureters, tied both and uremia developed.

Chevassu<sup>18</sup> reported a successful case in which the fistula followed a vaginal hysterectomy. The patient had had one attempt through the vagina, without cure. He considers it the operation of choice when the fistula is situated high in the vagina.

Marion, Segmund, and Chaput in discussing Chevassu's paper each reported a successful case.

DeCastro<sup>19</sup> closed a very extensive fistula by this method and seems to be the first to mention the lateral position during the postoperative period.

VonFranque<sup>20</sup> was rather enthusiastic in his paper, and felt that the operation had not received the credit it should. He successfully operated upon a patient on whom a vaginal attempt had failed. This writer also described the cases reported by Madelung, Koenig<sup>21</sup> and Baumm.<sup>22</sup>

Sippel<sup>23</sup> reports a failure operated in 1892 and states that the fistula was later closed from the vaginal approach at another clinic.

Stroeder<sup>24</sup> cured a fistula following hysterectomy, one vaginal attempt having been unsuccessful.

The largest number of cases has been reported from Marion's clinic. Davalos<sup>25</sup> in his thesis reported 15, 2 of which Marion<sup>27</sup> had reported elsewhere. He had used a linen purse string in the vaginal wall and one of catgut in the bladder. This seems to be the only clinic in which linen had been used. Marion also closed the suprapubic incision tightly and used only the indwelling urethral catheter for drainage. Of the 15 fistulas, 9 followed hysterectomy, 4 labor, 1 amputation of the cervix, and 1 was produced by an injury which tore the vaginal and bladder walls.

Binet and Grandineau<sup>26</sup> reported 1 case which had a fistula develop after operation for tuberculous disease. Two attempts were necessary for cure.

Perrin<sup>28</sup> reported 2 cases, 1 following a Wertheim operation and 1 an injury. No previous attempts had been made and both healed.

Kerr,<sup>29</sup> in closing the fistula in his patient, operated through the cystotomy

incision. He placed the sutures in the vaginal wall and closed the bladder wall from this approach, and then tied the vaginal sutures through the vagina.

H. McClure Young<sup>30</sup> obtained a partial cure with the Trendelenburg operation. A small fistula remained which he was subsequently able to close through the vagina.

Roeder,<sup>31</sup> although he does not perform the Trendelenburg operation, has operated upon 2 patients, using the suprapubic cystotomy wound. He dissected free, through the vaginal approach, 2 vaginal flaps which he sewed together through the cystotomy opening. He thus used vaginal mucosa to substitute for that of the bladder. His first patient, operated upon in 1919, was cured, but the second patient died on the eleventh day.

H. H. Young<sup>32</sup> successfully closed a fistula which had resisted eleven vaginal attempts to close. He used purse string sutures and prolonged suprapubic drainage.

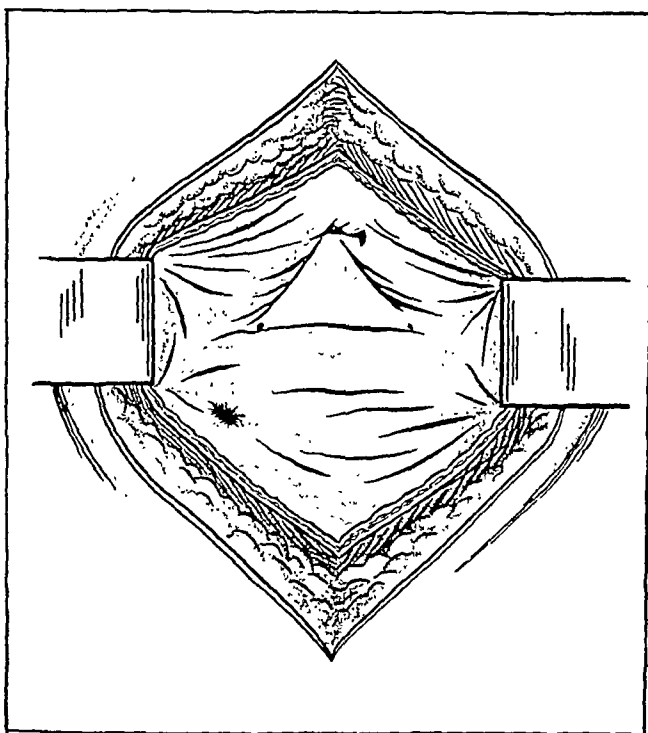


Fig. 1.—Bladder opened through suprapubic incision. Retractors in place. Fistula shown in base of bladder on the left.

### Report of my cases:

CASE 1.—Mrs. R. R., aged forty-six years, multipara. Seen November 28, 1927, with Dr. E. O. Boggs at Syracuse Memorial Hospital. Patient had had a repair and suspension operation two and a half years previously, and on September 9, 1927, had a complete hysterectomy for early adenocarcinoma of the body of the uterus. There was no evidence of bladder injury during the operation. Subsequently there was rather marked dysuria, requiring urinary sedatives, bladder irrigations, and installations. The urine showed pus constantly. On the tenth day while on a back rest, for the first time the patient noticed fluid coming from the vagina. This continued. Patient voided 200 to 300 c.c., but there was constant leakage through the vagina. On examination, November 28, a small opening about 8 mm. in diameter was found in the vagina leading into the bladder. It was found



to be located about 2 cm. superior to the left ureteral orifice. The operation was done in the following manner: Suprapubic cystotomy, the fistula was located and drawn up with hook tenaculum, the edges of the fistula were trimmed, separating the vaginal and vesical walls. The opening then was about  $1\frac{1}{2}$  cm. in diameter. With the index finger of the left hand in the vagina pushing the opening up into the wound, a purse string of No. 2 chromic catgut was placed in the vaginal wall, care being taken not to penetrate into the vagina. On tying this, the opening in the vaginal wall was snugly closed. A similar suture was then placed in the bladder musculature and tying this closed this layer leaving an irregular vent in the bladder mucosa. This was sewed with plain catgut No. 1. A large Pessar catheter was placed in suprapubic wound and wound closed as usual. The patient was kept on her abdomen for seven days, the suprapubic catheter left in for ten days. On the twelfth day postoperative, there was considerable leakage of urine from the vagina, the patient going home considerably discouraged. The drainage kept up

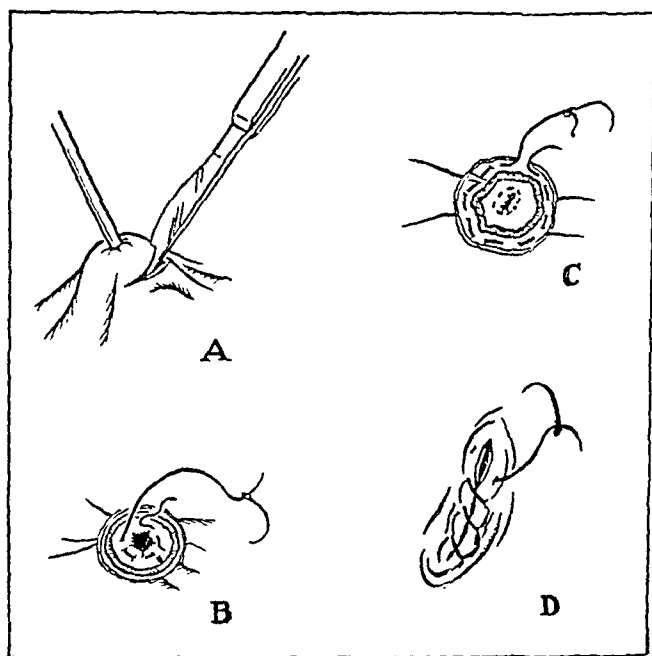


FIG. 2.—Semidiagrammatic drawings of the steps of the operation. (A) Fistula drawn up by hook. Denudation begun. (B) Appearance of fistula with denudation complete showing purse string of forty-day chromic catgut in the vaginal wall. (C.) Purse string in vaginal wall tied and similar suture placed in muscle wall of the bladder. (D) Closure of bladder mucosa with plain catgut.

about ten days and then stopped. The fistula has remained closed to date. I believe this leakage resulted from the use of twenty day catgut, and the fact that the suprapubic drain was not left in long enough. From the observation of this case and others, I must agree with Roeder who states that some fistulas result from damage done to the blood supply of the bladder at the time of operation and not to actual cutting or crushing of the bladder wall.

CASE 2.—Miss C. H., aged forty-nine years. Referred to me by Dr. Frederick Flaherty with the history that she had been operated upon for an intraligamentous myoma weighing  $15\frac{1}{2}$  pounds. During the operation it was known that the left ureter was cut. An attempt was made to transplant the cut end of the ureter into the bladder, but soon after operation there was leakage of urine into the vagina. My examination showed a small virgin vagina and on pressing down the perineum,

a large amount of fluid escaped. The speculum showed an opening 5 mm. in diameter very high in the left side of the vault. This I supposed to be the opening of a ureteral fistula. A ureteral catheter passed through this opening was seen on cystoscopy to be curled up in the bladder. The opening was definitely a vesicovaginal fistula. For some weeks I attempted to reestablish the lumen of the left ureter hoping to produce a functioning kidney on that side, but at no time was I able to get the smallest filiform to enter the ureter. No urine was seen coming from this orifice and repeated indigo carmine tests failed to show any function on this side. It was then decided to go ahead with the operation for fistula, leaving the left kidney as hopeless. The patient had no symptoms except the constantly leaking urine. Therefore, on February 3, 1928, a suprapubic cystotomy was done. The fistula which had been very difficult to expose by cystoscopy was easily seen. A self-retaining bladder retractor was adjusted. The edge of the opening was hooked up with a tenaculum and the mucosa trimmed away and the vaginal and vesical walls separated. A purse string of No. 2 "forty-day" chromic catgut was placed in the vaginal wall carefully avoiding any penetration of the vaginal mucous membrane. When this was tied the vaginal opening was snugly closed. A similar suture closed the bladder musculature and the mucosa was closed with plain No. 1. A large Pessar catheter was sewed into the suprapubic wound which was closed in the usual manner. The patient was kept on her abdomen for nine days, and the suprapubic drainage was maintained for nineteen days. There was never any leakage through the vagina and the fistula has since remained closed. The suggestion made by Dr. Flaherty that the fistula developed at the site where the attempted anastomosis of ureter and bladder was made seems most reasonable to me. Evidently the ureter pulled out leaving an opening in the bladder.

TABLE I. SUMMARY OF CASES FROM THE LITERATURE

AUTHOR	NO.	CURED	PART CURE	FAILURE	DEATH
Trendelenburg	3	1		2	
Willi Meyer	2			2	
MacGill	2	2			
Bordenheuer*	2	2			
Madelung**	1	1			
Baumm**	1		1		
Pousson*	1	1			
Rafin*	1	1			
Everke	3	2			1
Chevassu	1	1			
Segmund***	1	1			
Chaput***	1	1			
DeCastro	1	1			
VonFranque	1	1			
Koenig**	1				1
Sippel	1			1	
Stroeder	1	1			
Marion	15	15			
Binet	1	1			
Perrin	2	2			
Kerr	1	1			
H. McC. Young	1		1		
Roeder	2	1			1
Hugh Young	1	1			
Sears	2	2			
Farman	1	1			
Total	50	40	2	5	3

\*Quoted from Thiers.

\*\*From VonFranque.

\*\*\*Reported while discussing Chevassu's paper.

Since the material for this report was accumulated, Farman and Thompson<sup>33</sup> presented a case in which they successfully closed a fistula by the Trendelenburg operation. The patient was first treated by an indwelling urethral catheter and fulguration of the fistulous opening. This failed and an effort was then made to close the fistula through the vagina. This also failed and it was then that the suprapubic operation was successfully done.

#### SUMMARY

I have collected from the literature 48 cases of fistula treated by the suprapubic transvesical operation, and to these, have added two more. It will be seen that 40, or 80 per cent of the cases have been cured. There are 2 classed as partial failures. It might be argued that these should be grouped with the failures since the suprapubic operation failed to close the fistula. It seems, however, that this procedure was indirectly responsible for the cure, since it so much improved the condition as to permit easy closure through the vagina.

There were 5 failures. All of these occurred during the early history of the operation. In 3 of these the surgeon resorted to colpocleisis after one attempt, and in one the vaginal canal was closed after two attempts. In Sippel's patient a vaginal operation later was successful.

There were 3 deaths. In 2 of these, the fistula was extensive; the surgeon failed to put catheters into the ureters and both were tied, death occurring from uremia in one, and following a second operation to relieve the ureteral obstruction in the other. The third death occurred on the eleventh day but the cause was not stated.

Four cases developed vesical stone. In 3 instances a suprapubic operation was performed to remove the stone and in the other the stone was removed per urethram.

A fistula between the urethra and the vagina complicated the vesicovaginal opening in 2 cases.

Many of the patients had had several attempts to close the fistula through the vagina; in 1 there had been 11 such operations. A second suprapubic operation was needed in only 3 of the cured cases.

#### CONCLUSIONS

From the above review it may be concluded that:

1. A suprapubic transvesical operation will cure a high percentage of vesicovaginal fistulas, even when many vaginal attempts have failed.
2. It gives much better access to any fistula fixed high in the vagina, especially if the uterus has been removed.
3. When the ureters are in danger of ligation, ureteral catheters should be inserted during the operation.
4. The technic may vary according to the size and condition of the fistula, but careful separation of the bladder and vaginal walls followed by their proper approximation is essential.

5. "Forty-day" chromic catgut, linen or silkworm gut should be used in the vaginal wall, "forty-day" chromic catgut in the bladder musculature and plain catgut in the bladder mucosa.

6. No suture should penetrate the vaginal wall, so that "stitch hole" fistulas may be avoided.

7. Suprapubic drainage should be maintained for two or three weeks, although DeCastro and Marion closed the bladder tightly with excellent success.

8. Either the lateral or the prone position seems advisable during the postoperative period.

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## A CASE OF RUPTURED UTERUS FOLLOWING CLASSICAL CESAREAN SECTION

By EDWARD L. CORNELL, M.D., F.A.C.S., CHICAGO, ILL.

THIS patient, J. K., was operated upon by me at the Cook County Hospital, April 25, 1928. She was a para ii, aged 20, white, and was first examined in the prenatal clinic, February 27, 1928. Her last menstrual period was August 28, 1927. In her previous pregnancy at the eighth month she was operated upon at another hospital for a typical case of abruptio placentae. A classical cesarean section was done August 14, 1926. The baby died when a week old. She reported to the prenatal clinic every two weeks and complained only of indefinite symptoms, such as backache and some abdominal discomfort. At one visit a diagnosis of mild polyhydramnios was made. Her blood pressure was always within the normal.

On the twenty-fifth of April, five weeks prior to her calculated date, the patient began to have pains at 6:00 A.M. She entered the hospital at 8:30 A.M. with a temperature of 96° and a pulse of 108. On admission, examination showed that the cervix was closed and that the head was floating. The position was O.L.A. She was complaining of mild abdominal pains especially over the line of incision of the previous cesarean section. This area was quite tender. The fetal heart tones were heard on admission but could not be distinguished three hours later. The round ligaments were not tense, and the uterus was not contracting very vigorously. The pain over the incision became progressively worse. A vaginal examination at 11:00 A.M. under strict asepsis revealed a long cervix (2 to 3 cm.) with no dilatation. The patient was advised to have an immediate cesarean section and the operating room was prepared for her reception. At 11:45 A.M. my colleague, Dr. D. A. Horner, saw the patient and confirmed the diagnosis of a threatened rupture of the uterus and strongly advised the patient to be operated upon. At the time of his examination the baby was in the uterine cavity and the abdomen was soft. The pain over the old abdominal incision was quite severe. The incision was exceedingly tender. The patient absolutely refused to be operated upon at that time in spite of the fact that she was warned. She insisted on getting up to telephone her mother to come and remove her from the hospital. Her condition became progressively worse, her pulse more rapid and thready. At 3:30 P.M. when I saw the patient she was in beginning shock. At that time the abdomen was quite rigid, no fetal heart tones could be heard and it was impossible to outline the fetus. At this time she consented to be operated. Under a very light ether anesthesia the abdomen was opened. The patient died very shortly after this was done. The saline solution was started by hypodermoclysis as soon as she was in the operating room.

On opening the abdomen we found a large adhesion between the uterus and abdominal wall. The adhesion was filled with blood which distended it so that it was almost the size of a fetal head. The fetus enclosed in the intact membranes and placenta was found in the upper left side of the abdomen. The uterus was poorly contracted and located in the lower abdomen in the median line. The abdomen was filled with blood, estimated at 1000 c.c.

After removing the fetus and membranes the uterus was examined. The adhesion was attached practically the entire length of the abdominal wound and also the uterine wound. The original tear in the uterus undoubtedly started near the lower end of the classical section scar and extended upward, but as soon as the baby was

expelled it was carried beyond the confines of the old scar because the uterus was torn throughout the length of its body. It was the largest rupture I have ever seen. The uterus was removed.

It was remarkable that this patient did not have a sudden sharp lancinating pain when the uterus ruptured and expelled the fetus. Since everyone in the hospital was anxious about the patient, the nurses and interns were on the lookout for early signs of a definite rupture but the patient gave none.

122 SOUTH MICHIGAN AVENUE.

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## SPONTANEOUS SEVERANCE OF UMBILICAL CORD\*

BY LOUIS H. DOUGLASS, M.D., F.A.C.S., BALTIMORE, MD.

THIS case is presented solely because of its apparent rarity, since none of the standard textbooks which the author has seen, mentions it. A careful search of the literature shows no similar case and only one which is in any way analogous; that of Funke, who believes his to be the first case reported in the literature. It is of scientific interest only, since there seems to be no clinical lesson to be learned, no way in which a diagnosis could be made, and no treatment which would prevent.

Mrs. L., a para iii, thirty years of age, was seen at her home on the evening of Feb. 24, 1929, in consultation. The physician in attendance asked me to see her because of a suspected transverse presentation. He said that one week ago abdominal palpation showed an apparent vertex presentation, but that when he saw her after she had been in labor for four to five hours, and examined her vaginally, he felt a small part, which he thought was a hand. The patient's past history is not significant, her family history is negative, her husband's health is good and he denies any venereal infection. Both previous pregnancies and labors were normal. The first baby weighed  $4\frac{1}{2}$  pounds at birth and the doctor at the time remarked that the placenta was very large. No abnormalities at the second birth; both children living and well, the oldest being three years and the youngest fourteen months. Wassermann positive.

The present pregnancy presented no marked symptoms to the mother. Her last menstrual period was May 21, 1928, which would bring her to term early in March or about one week after the actual labor. Fetal movements were first felt at the usual four and one-half months, and she said that they continued until the day of delivery, remarking later that they were never very strong (a statement which later findings proved wrong). When I saw the patient she had been in labor for six or seven hours and the pains were three to four minutes apart and fairly strong. Upon inspection the abdomen was greatest in its transverse diameter, the height of the fundus being 24 cm. There was a marked separation of the abdominal muscles. No fetal parts could be felt, there appeared to be a large amount of amniotic fluid and fetal heart sounds could not be heard. Rectal examination was negative and therefore a vaginal examination was made. The external os was dilated about 5 cm. and a distinctly bulging amniotic sac was protruding through it. Within this sac a small part could be felt, which appeared to be about

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\*Read before the Obstetrical Society of the University of Maryland.

the size one would expect in a pregnancy of fourteen weeks' duration. It was not possible to tell whether it was a hand or a foot at this time. Labor was allowed to continue for one and one-half hours, when, since there was no advance, it was decided to interfere. The patient was anesthetized and prepared in the usual manner. A vaginal examination with the whole hand in the vagina now showed that the small part previously felt was the foot and not the hand. The membranes were ruptured artificially and a large amount of dark brown amniotic fluid escaped, the color being that which one usually associates with a dead fetus, but not at all suggestive of blood, either fresh or old. A simple breech extraction was done and a dead baby delivered. Shortly after delivery the patient began to bleed rather freely, and since the uterus did not contract well, a manual removal of the placenta was thought advisable, and was done. The placenta was normally implanted, not firmly adherent and peeled away easily. After removal the uterus contracted well and bleeding was controlled. Patient's condition was satisfactory and remained so.

The child was apparently of about twenty-eight weeks' gestation, weight, 1125 gm., length, 29 cm. The head was apparently normal except that there was some overlapping of the bones of the skull commonly seen after fetal death. The trunk and arms were normally developed, but the lower extremities were very short, thin and puny. Growth of these parts had apparently ceased some time prior to the death of the child.

When the child was delivered I automatically reached for a clamp to clamp the cord, but was very much surprised to find that there was no cord protruding from the vagina. I then looked at the baby and found that there was a stump of cord which later was found to measure  $7\frac{1}{2}$  cm. in length and to be of normal thickness and consistency. The end tapered slightly and was completely sealed over, there being no raw surface.

The placenta was very large and pale, weighing 1565 gm., but there were no infarcts or other abnormalities noted. The cord was inserted centrally, measured 14 cm., giving a total cord length of 21.5 cm., and tapered as did the fetal portion. The tip was also sealed over and it was evident that separation had taken place several weeks prior to birth. The membranes were perfectly normal and intact, showing only the one rent which was made at the time of delivery.

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## DOUBLE RENAL DECAPSULATION FOR PUERPERAL ANURIA

By IRVING B. KRELLNSTEIN, M.D., F.A.C.S., NEW YORK, N. Y.

**T**HIS case is that of a woman who had complete anuria following the birth of a stillborn fetus at term with recovery after a decapsulation of both kidneys.

Mrs. R., aged thirty-three, was admitted to Lebanon Hospital, August 22, 1927, with marked vaginal bleeding and severe labor pains. Her last period was November 15, 1926, the expected date of confinement was August 22, 1927. The patient was a para ii. Fourteen years previous she had had an induction of abortion for pernicious vomiting of pregnancy. Two years later she had a normal delivery. She had measles and scarlet fever when a child. In 1925 the patient was operated upon for acute appendicitis. On admission, the patient stated that she felt no fetal movements since day previous. Our examination showed a well-developed woman with normal pulse, temperature and respiration, and slight edema of hands and feet. Blood pressure 145/95. Cervix was two fingers' dilated, thin, with no evidence of a low implantation of a placenta. Bladder contained no urine upon catheterization. During the five months that the patient was under my care, she was on a restricted diet and experienced no abnormal vomiting, spots before her eyes or headaches, and had never shown any marked evidence of kidney impairment. Urine examination showed a trace of albumin, no sugar, acetone, blood, or casts. Blood pressure ranged between 114/40 and 132/50. She had slight swellings of hands and feet. Patient was delivered by medium forceps about four hours after admission of a stillborn baby. Placenta showed signs of partial separation, which in all probability was the cause of fetal death.

Immediately following the delivery, the patient complained of dimness of vision. August 26, four days after delivery she was cystoscoped. The bladder was moderately inflamed and empty. No obstruction in either ureter, for catheters passed freely to both kidneys but drew no urine. In the afternoon, with the aid of Dr. Abraham Hyman, bilateral decapsulation was done. At operation each kidney was found slightly enlarged, pale and friable. Capsule easily stripped from kidneys. About twelve hours after operation four ounces of urine were obtained from the bladder. Two days later, August 28, 270 c.c. were obtained, August 30, 380 c.c., and subsequently a normal amount. Urine for the first three weeks contained a heavy trace of albumin and occasional granular and hyaline cast, which later disappeared.

Blood chemistry on August 23, day after admission, showed NPN. 29; urea N. 14; uric acid 1.8; sugar 99. All this increased in subsequent examinations, when the highest was reached on September 9, NPN. 127; urea nitrogen 80; uric acid 10.3; creatinine 14.1. Following this last examination, the blood chemistry improved and on October 28 was, NPN. 57; urea nitrogen 37; uric acid 4; creatinine 4.1; sugar 114. Blood pressure ranged between 145/95 to 180/104. At present blood pressure is normal. Blood count showed Hg. 50 per cent; R.B.C. 2,500,000; white blood cells 18,000; polynuclears 82 per cent; lymphocytes 18 per cent.

Patient was drowsy and at times irrational. Vomited large amounts and rather frequently, complained of violent headaches and blindness of vision. The patient was free from fever except once when the temperature rose to 104° following an intravenous injection of 10 per cent glucose solution.



Her treatment consisted besides the bilateral decapsulation, of colonic irrigations, proctoclysis, and intravenous injection of glucose solution.

#### SUMMARY

This is a case of complete suppression of urine lasting four days, due to a recent toxic degenerative nephritis, which was relieved by bilateral decapsulation.

I wish to thank Dr. Abraham Hyman and Dr. Sidney Steiner for their assistance in this case.

1022 FAIRLIE STREET.

### A NEW PELVIMETER

BY HARRY STUCKERT, M.D., PHILADELPHIA, PA.

WHEN performing external pelvimetry one desires to take the pelvic measurements expediently and cause the least amount of annoyance and discomfort to the patient.

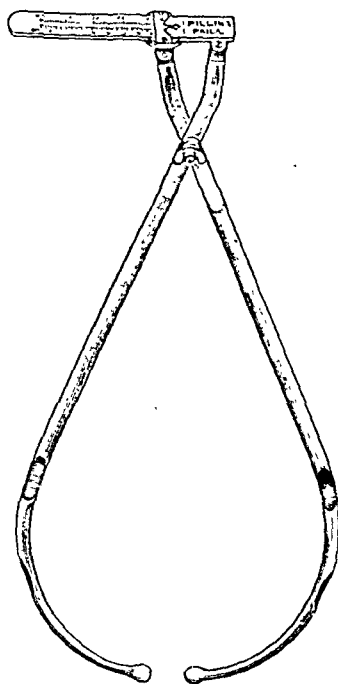


Fig. 1.

Fig. 1 represents an instrument which the George P. Pilling & Son Co., Philadelphia, made for me. It enables all external measurements to be taken with ease, the patient being either in the recumbent or standing position.

The reading scale is so situated as to be in perfect view at all times, and it matters not which side of the instrument faces the operator, or at what angle it may be held, the scale is still easily read.

# Society Transactions

## OBSTETRICAL SOCIETY OF PHILADELPHIA

*STATED MEETING, DECEMBER 6, 1928*

### DR. ROY W. MOHLER described a case of Postpartum Eclampsia Following a Previous Nephrectomy.

Mrs. K. aged thirty-four, last menstrual period August 26, 1927. Menstruation began at fifteen, occurred every thirty days, lasted four days with a moderate flow and with pain on the first day. She married at the age of twenty-seven and had one pregnancy in 1923, which was terminated by a forceps delivery. She said she was very sick but her history did not suggest a fever or toxemia. For a short time she complained of a slight white vaginal discharge, aside from this she was perfectly normal.

The family history did not suggest a predisposition to any chronic diseases.

In 1918 she had influenza and in 1925 she had a left nephrectomy for pyonephrosis, the history of this infection dating back about five years. Since the operation, she had been perfectly well. The function of the right kidney was normal until one week before delivery.

During her pregnancy her blood pressure remained 130/85, her weight increased about 40 pounds. One week before delivery she developed a temperature of 100.6°, with pains all over the body and head and swelling of her ankles. The urine contained many pus cells, no casts and a cloud of albumin. She had some tenderness over her right kidney. The diagnosis at this time was right pyelitis. Her temperature and physical findings did not change until May 21, 1928 at which time she went into labor. Two hours after the beginning of labor her temperature became normal and remained so until the sixth day postpartum. Her labor was normal and easy, lasting about five hours, with a very moderate loss of blood, and a living child.

During the morning of the fourth day postpartum, May 26, 1928, her blood pressure ascended to 180/100, on the fifth day she complained of spots before her eyes, a headache and her blood pressure was 194/105, and at 10:30 A.M., she developed an eclamptic convulsion. At 3 P.M. she received 10 c.c. of heparmone intravenously which increased her headache to the point almost of intolerance. A few minutes after the injection her headache subsided some and in ten minutes we repeated the 10 c.c. dose of heparmone intravenously, at 3:15 P.M. she had another convulsion. Her blood pressure came down considerably after the second convulsion and at 7 P.M. she had another convulsion. The sixth day her blood pressure was considerably lower and she felt pretty well. On the seventh day her blood pressure was 130/85, the same as it had been throughout her pregnancy. After the seventh day her blood pressure began advancing and she had a recurrence of her headache and spots before her eyes. Heparmane was given 10 c.c. twice daily intramuscularly but the blood pressure gradually ascended to 210/120 on the ninth day. After each injection of heparmane her blood pressure would drop about 20 points and there were no bad effects from its use intramuscularly. After the ninth day her blood pressure began to descend, on the eleventh day it was 154/100 and finally descended to 126/74 on the seventeenth day postpartum.

The blood chemistry was normal, uranalyses throughout her illness showed albumin ranging from a faint trace to a light cloud, granular casts at times and considerable pus. The temperature ranged from 101° to normal from the fifth to the eighth days postpartum.

On the seventeenth day postpartum she was discharged from the hospital, with normal blood pressure. The urine contained a faint trace of albumin, with no casts and a few pus cells. Her weight decreased about forty-five pounds. Since leaving the hospital she has been perfectly well.

This patient was given 80 c.c. of heparmone, the first two doses intravenously. Due to the convulsion which immediately followed and apparently caused by its use, this was discontinued for three days. On the ninth, tenth, and eleventh days she received two doses of 10 c.c. each of heparmone intramuscularly with a marked lowering of her blood pressure following each dose. Beside the heparmone she received every four hours ½ ounce of glucose in the juice of one orange and plenty of fluids, plus the usual run of sedatives in moderately large doses.

This case is particularly interesting because the patient had had a previous nephrectomy, and the eclampsia did not develop until five days after delivery. It is probable that the eclampsia was induced by the attack of pyelitis which developed one week before delivery. It is also interesting because of the reactions in this case produced by the heparmone injections.

DR. GEORGE P. PITKIN read, by invitation, a paper entitled **Spinal Anesthesia in Obstetrics and Gynecology**. (For original article see page 165.)

#### DISCUSSION

DR. JOHN B. DEEVER said there were given over 4,000 spinal anesthetics in his clinic, of which spinocaine was used in 443. There is no question of the superiority of this type of anesthesia in selected cases.

DR. WAYNE BABCOCK felt that Dr. Pitkin had perhaps done more in the last two years, than any other man in this country to popularize the method and attempted to bring almost micrometer precision in the use of spinal anesthesia so that it may be accurately limited to certain parts of the body. During pregnancy, however, the use of spinal anesthesia is not free from risk, especially in less skilled hands.

There are four things to be emphasized in giving the intradural injections: first, the force of the injection. If done with force the solution will go to a higher level than you anticipate. If you can keep it below the level of the second lumbar segment you will have no effect on the blood pressure, because only above the second lumbar segment lie the sympathetic fibers. If the anterior nerve roots are blocked above this point there will occur a fall in blood pressure which increases progressively until with the second thoracic segment, the cardiac contraction becomes slow and feeble, and the pulse may disappear from the wrist. If the external muscles which are used in respiration are deprived of function, the patient must live by the use of the diaphragm, but in advanced pregnancy the diaphragm is so splinted by the greatly enlarged uterus, that the patient, unless relieved by artificial respiration or the immediate emptying of the uterus, may die of asphyxia.

Spinocaine solution diffuses rather slowly, but not as slowly as a similar solution with the viscid or starch element removed. The spinocaine diffused more rapidly in five minutes, four hours, twelve hours, than did simple anesthetic solution containing a comparable content of alcohol. Dr. Babcock believed that perhaps Dr. Pitkin had been misled in thinking that the slow diffusion of his

solution was due to the starch, when it is really due to the alcohol. But after all, if there is not sufficient diffusion to block every nerve root supplying the operative field, the anesthesia will not be satisfactory. A degree of diffusibility is essential for dependable anesthesia.

A second important point is the bulk of solution injected. Higher and more widespread effects are produced by increasing the quantity of the fluid that is injected. A third point is the amount of cerebrospinal fluid withdrawn; if much is first withdrawn and the dura thereby decompressed, a higher analgesia will result. Fourth, the specific gravity of the solution in relation to the position in which the patient is placed greatly influences the location of the anesthetic, although not as much as the location of the interspace selected for the injection. If the drug is not in excess it will soon fix itself to the nerve elements, and after ten minutes the area of anesthesia can rarely be changed. No manipulation of the patient will then modify the effect, unless there is an excess of the spinal anesthetic or something which prevents the attachment of the drug to the nerve roots.

All four of these points should be considered whenever spinal anesthesia is given, and one may again recall Dr. Pitkin's precision in technic. But the large dose of procaine in heavy solution which he recommends in obstetric operations is not free from danger. Ninety-eight or 99 of such injections may have no serious complication, but in the hundredth a serious collapse and death may occur unless special precautions are taken. With an obstetric patient so often restless and thrashing around in bed there is a special hazard when an excess of the anesthetic is within the dura.

Dr. Babcock considered that spinal anesthesia should not be used except in a well-appointed hospital and with the presence of associates well trained in the methods of resuscitation. There are three things which are sheet anchors when the patient appears about to die from the intradural injection: first, adrenalin by vein or heart to stimulate the circulation (ephedrin is not dependable in the dire emergency); second, artificial respiration, if necessary, by mouth to mouth insufflation, and third, maintenance of the temperature of the body.

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## OBSTETRICAL SOCIETY OF PHILADELPHIA

*STATED MEETING, JANUARY 3, 1929*

DR. LEOPOLD GOLDSTEIN reported a case of **Microcephalic Idiocy Following Radium Therapy for Uterine Cancer During Pregnancy**. (For original article see page 189.)

### DISCUSSION

DR. D. P. MURPHY said that within the last few days he had seen still another case of microcephaly, apparently produced by therapeutic roentgen irradiation during pregnancy. He favors the belief that the microcephalic children as reported upon in the literature, together with the two which he personally observed were the direct result of the roentgen irradiation received in utero.

The chief question is whether or not to use the curette before pelvic irradiation. Dr. Murphy claimed that if curettage is always performed before treatment with the roentgen ray, fewer microcephalic children will be born.

DR. F. E. KEENE said that as the results of the investigation here reported, there are certain points which are of extreme importance to those using irradiation therapy. Apparently, from their review of the literature we are warranted in

assuming that a child born after irradiation, in other words in the so-called pre-conception stage, will be a healthy child. Apparently the integrity of the ovum is not impaired by irradiation at that time. On the other hand, the ill effects are frequently shown when irradiation has taken place at the time of pregnancy and this applies particularly when radiation has been used during the early months of pregnancy. Their work has shown that the *anlage* of the central nervous system is particularly susceptible to x-ray or radium, so that in a considerable proportion of cases this defect is represented by microcephalic idiocy.

As to the case itself which forms the basis of the report of Goldstein and Murphy, this patient had been bleeding for four months prior to coming to the hospital. During the last two weeks of that time she was confined to bed on account of the bleeding; it was impossible to determine exactly what the term of pregnancy was but it was believed to be between six and seven months. Because of this patient's general condition, operation was out of the question. She presented a sloughing, ulcerated, easily bleeding mass, occupying the left side of the cervix, about two inches in diameter and definitely pedunculated. In order to control the bleeding, Dr. Keene applied a clamp and removed the mass with a cautery. One hundred and eighty-five mg. of radium were applied and left in place for twenty-four hours, as a palliative measure. He anticipated spontaneous emptying of the uterus. However, such did not occur. She was instructed to return in six weeks. It was thought that in all probability as cesarean section would be necessary. She returned in five weeks, at which time the cervix was almost completely dilated, and she was delivered by Dr. Barton Cooke Hirst of what was apparently a normal child, without complications. Following delivery, Dr. Hirst made a second application of radium, using 85 mg. for twenty-four hours.

The presence of a carcinoma and pregnancy in a young woman usually means a rapidly fatal termination, but it is now twelve years since she was treated and at a recent examination there was no evidence of malignancy.

Dr. Keene wanted to emphasize Dr. Murphy's remark dealing with the importance of eliminating pregnancy in irradiation treatment of myomas. Of course when intrauterine applications are made, this is always preceded by a careful examination under anesthesia and a diagnostic curettage. Hence, the chief danger comes with those patients who are subjected to x-ray treatment. It is extremely important, therefore, that the radiologist work in conjunction with the gynecologist to rule out this possibility.

The question arises as to whether or not one is justified in carrying out diagnostic x-ray examinations in the presence of pregnancy. Such examinations can be safely made. On the other hand, when x-rays are to be used therapeutically for extrapelvic lesions, the presence of pregnancy must be definitely ruled out, because in prolonged irradiation, injury to the developing fetus can readily occur.

DR. F. E. KEENE in answering Dr. Williams, as to what procedure should be adopted during the latter months of pregnancy complicated by carcinoma of the cervix, it seemed to him that the procedure carried out by Dr. Williams is the only one available.

DR. PHILIP F. WILLIAMS had seen two cases: one a woman in the early forties who had bleeding from the uterus; diagnosis showed no carcinoma of the fundus and the cervix was normal. She received roentgen treatments over a period of time, about seven to nine treatments, and finally the menstrual flow diminished in duration and then for several months it was only for one day or a part of a day, and it then ceased. She thought artificial change of life had been produced, and then some months later was found to be four months pregnant. She went through the pregnancy normally and produced a healthy child, which has since been growing in a normal manner.

Another point is what are we to do when confronted in late pregnancy with inoperable carcinoma of the cervix? Such a patient came to the Abington Memorial Hospital; she was seven and one-half months pregnant and had an inoperable cancer of the cervix; she was exsanguinated. Dr. Williams did a cesarean section at once and then used 2400 millicurie of radium. The cervix healed over almost entirely and it was difficult to get her to return to clinic for follow-up study. Eventually he found some metastasis in the pelvis.

DR. WALTER F. HARRIMAN read a paper on **The Treatment of Endocervicitis with the Actual Cautery and Electrocoagulation.** (For original article see page 250.)

DRS. LEWIS C. SCHEFFEY AND WILLIAM H. SCHMIDT presented a paper on **Diathermy as an Adjunct in the Treatment of Pelvic Inflammatory Disease.** (For original article see page 233.)

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## CHICAGO GYNECOLOGICAL SOCIETY

*STATED MEETING, NOVEMBER 16, 1928*

DR. CHARLES EDWIN GALLOWAY reported a case of **Osteogenesis Imperfecta.**

The patient had a breech presentation and what was practically a normal labor, lasting about seven hours. When she reached complete dilatation, she was anesthetized with drop ether and extraction started. The leg came down very easily. As he made traction on the foot it snapped. The arms came down very easily. When he made a little pressure on the head, he felt it give as though he had indented a cranial bone. After delivery the noticeable thing about the baby was that the body was quite long. The legs were quite short but the upper extremities were normal. The head was misshapen, probably due to its position in the uterus. X-ray examination a few hours later showed a definite fracture of the left femur, a fracture of the right femur near the upper third, and a dislocation of the left shoulder. The head felt very much as though there were a fracture of the occipital bone. It was a case of osteogenesis imperfecta, characterized by abnormal length of the body and short, lower extremities. The interesting part about the case is that the x-ray showed that the right femur was fractured while in utero and had healed with some deformity. A case of osteogenesis imperfecta is very seldom seen at birth. The Wassermann on both parents was negative. The pregnancy was perfectly normal.

DR. A. E. KANTER reported a case of **Tubal Torsion.**

Mrs. P., aged forty-seven, came to the Cook County Hospital complaining of pain in the lower left quadrant which came on suddenly, ten days ago. At that time she began to feel dizzy and had severe sharp knife-life pains which were aggravated by motion. Menstruation was regular up to January 19, she missed February, menstruated regularly during March and April, then missed May, June, July, and August. September 4, she had a severe hemorrhage using 10 or 12 pads daily for seven days. October 6 she began to bleed again, the hemorrhage continuing for six days, using 10 pads daily. She had had six pregnancies; one full-term delivery twenty-seven years ago, one premature labor, 4 others being terminated at two months (self-induced).

Bimanual examination showed a nodular lacerated cervix with erosion, uterus enlarged, hard, anteflexed. Right adnexa apparently negative. Mass felt through left fornix.

Laparotomy revealed an enlarged uterus in good position. Right ovary and tube normal. Left ovary normal. Left tube enlarged, clubbed end, purplish in color, and twisted upon itself three times. Attached to the tube was the omentum which prevented the tube from straightening itself. The omental adhesions were separated from the tube very easily, showing that they were of recent origin. Evidently the tube was a hydrosalpinx which became a hematosalpinx after torsion.

DR. RIES said that he had presented a similar specimen to the Society in 1897.

DR. EMIL RIES reported a case of **Sampson's Tumor of the Endometrium**.

The patient was twenty-two years old, with symptoms of chronic appendicitis and a history of two acute attacks within a short period. There were no other symptoms. Menstruation was regular and normal. On examination there was a tumor back of the cervix, but not connected with the cervix, with the vaginal mucosa movable over it and the rectum free. The tubes and ovaries were separated and could be palpated distinctly. The tumor was hard, nodular and the size of the long phalanx of the little finger. Rectal examination showed the rectal mucosa movable.

The question arose as to what sort of a tumor this was. If it were observed in an old lady who possibly had a carcinoma of the stomach or of some other abdominal organ, one would think of metastasis in the culdesac. Because of the youth of the patient a carcinoma was not suspected. A diagnosis was made of Sampson's tumor of the rectovaginal septum. When removed the tumor was full of black spots. It was an adenoma of the rectovaginal septum. They may become fused with the anterior wall of the rectum and the uterus to such an extent that some operators have removed the rectum and uterus and made an anastomosis. It has recently been shown that this tumor responds to x-ray treatment. Operations for large tumors in this location which become fused with the rectum and uterus are very difficult. This tumor was removed per vaginam without opening the peritoneum. The abdomen was then opened, the appendix removed, and the tubes, ovaries, and uterus inspected. There were no black spots. The culdesac had a few adhesions. There was no history of peritonitis except these attacks of appendicitis. The gall bladder was free, there was no tumor in the stomach, and nothing in the right kidney or ureter.

DR. EDWARD ALLEN presented a specimen of **Ovarian Tumor**.

The patient had a gastric resection for carcinoma of the stomach, and she had bleeding from the uterus for two months. These tumors were felt at this time, and about 2 or 3 cm. in diameter. They were diagnosed as ovarian tumors possibly secondary to a lesion in the stomach. When the patient came in a month later, they were considerably larger. When she returned subsequently, bleeding considerably, the tumors were removed. They were ovarian growths, probably Krukenberg in type. There was nothing in the culdesac.

DR. CARL HENRY DAVIS read a paper on **Leucorrhea**. (For original article see page 196.)

#### DISCUSSION

DR. J. P. GREENHILL was interested to learn that Dr. Davis had found 38 private patients with *Trichomonas vaginalis* in the past ten months, and that he had stressed the necessity of making routine hanging drop examinations in every

patient with a leucorrheal discharge. But he had not found it necessary to add any salt solution. The hanging drop is taken from the material found on the rubber glove, placed on a glass slide and examined. The central portion of the drop is very thick; one can seldom make out anything but pus. At the periphery, however, actively motile trichomonas can easily be distinguished. Dr. Greenhill agreed with the criticism of the various methods used in treatment. In a series of 56 private cases, some of which were followed up as long as three and four years, Dr. Greenhill obtained cures in almost 90 per cent. His method is to first scrub the vulva and the vagina with green soap until there is a slight bleeding in the mucosa. The soap is washed out with water and the vagina is then dried. A tampon saturated with a mixture of glycerine and a weak solution of methylene blue is inserted into the vagina. Green soap and glycerine destroy the organisms very quickly, just as Dr. Davis found experimentally.

Dr. Davis' experiments showed that methylene blue required fifteen minutes to kill the trichomonas. In cases of *Trichomonas intestinalis*, Castellani recommends taking methylene blue by mouth, and also irrigations of the large intestines with methylene blue. In Dr. Greenhill's procedure the methylene blue plays only a small part, for in the solution used by him there is more than 25 times as much glycerine as methylene blue and the glycerine is much more important.

Dr. Greenhill had used lysol and phenol douches in the treatment of trichomonas as suggested by Dr. Hegner but so far he is not convinced that they are better than lactic acid. His plan is to discontinue the office treatment after finding two consecutive negative slides, but the patient is instructed to continue the lactic acid douches for a number of weeks longer.

DR. W. C. DANFORTH said the frequency with which the *Trichomonas vaginalis* is found is not generally appreciated. He had not kept count of the number he has seen this year, but is certain it is more than 38. He tried various methods of treatment, some of which the essayist outlined, with satisfactory results in relieving the immediate consequences of the infection. He tried the method outlined by Dr. Greenhill in his paper last winter, but instead of using lactic acid in a good many cases he has used soap douches. He has also treated some by the use of mercurochrome followed by glycerine tampons or by a tampon of sodium bicarbonate or Fuller's earth. All these methods seem to give pretty good results so far as the immediate effects are concerned. The problem is the recurrence. Most of the cases he has seen with satisfactory cures come back with recurrences, some of them with several attacks. He hoped that Dr. Davis' studies in the life cycle of this organism will give some light on a method whereby permanent results may be obtained.

DR. DAVIS, in closing, said his paper was primarily on leucorrhea. He emphasized trichomonas because that is one factor in leucorrhea which has not been given sufficient consideration in the past.

His feeling regarding glycerine and methylene blue is that the glycerine does the work and the methylene blue gives only color. His opinion in this respect is confirmed apparently by his experimental work.

The various workers in the field of protozoology are all agreed that they do not know much about trichomonas. They do not know how to get rid of it from the intestinal tract. They do not know whether the *Trichomonas vaginalis* is the same as the *Trichomonas intestinalis* or not. He tried to find the parasite in the stools of patients who had *Trichomonas vaginalis* but so far had not been successful. It has recently been suggested that it is necessary to give a cathartic so that fecal materials will be carried through rapidly.

Dr. Greenhill may be perfectly satisfied in using the undiluted drop, but in so doing he may have overlooked many cases of *Trichomonas vaginalis*. Patients



under treatment are checked up immediately after menstruation, and Dr. Davis is not satisfied to say the examination is negative, unless he has searched for several minutes and not found a single trichomonas. If a single organism is found, treatment must be continued. He does not feel that any one can call a patient cured until he has examined her after menstruation for several months. Then, if none are found, the chances are that she is cured. Because these patients may have an associated intestinal infection, he advises them to wash with soap and water after stools, before coitus, and frequently during menstruation while they are wearing a pad.

DR. A. G. GABRIELIANZ (by invitation) presented a paper entitled, **Endocrines in Gynecology, With Special Reference to Dysmenorrhea and Other Menstrual Disturbances.**

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## CHICAGO GYNECOLOGICAL SOCIETY

*STATED MEETING, DECEMBER 13, 1928*

DR. ROBERT M. GRIER presented a paper entitled, **A Study of Fifty Consecutive Ectopic Pregnancies.** (For original article see page 240.)

### DISCUSSION

DR. N. SPROAT HEANEY said he should like to see a study brought out which separates the ruptured cases from the unruptured, since there is as much variation as there is between pregnancy in a normal uterus and in a ruptured uterus. He said that Dr. Grier's experience agreed with his own, that the most important and frequent symptom is irregular bleeding, while amenorrhea is only second and pain stands third. In textbooks the sharp lancinating pain of a ruptured ectopic is so vividly described that the novice feels that pain is the predominating symptom in the consideration of the diagnosis of ectopic pregnancy, and in consequence is loath to diagnose a suspicious case as ectopic until the tragedy of a rupture occurs. He had seen at least one case where not the slightest pain or discomfort could be elicited in an inquiry into the history.

DR. CAREY CULBERTSON said that the term ruptured ectopic pregnancy as it is ordinarily used is a term which has come to mean an intraperitoneal spill of blood in connection with a pregnancy. It has been the custom in past years to think of pain as the commonest symptom but as Dr. Grier's study shows and as Dr. Allen's recently reported series of 49 cases shows, metrorrhagia is the most frequent sign, more frequent than any of the other symptoms. Dr. Grier's report again shows the absence of amenorrhea in about the usual number of cases, always an interesting observation. On the other hand, his series shows a larger percentage of cases with shock and collapse than is usual. In Dr. Culbertson's cases this had been exceedingly rare, though he had seen syncope where only a small amount of blood was present in the pelvis. Hence, while creating an appearance of crisis and compelling emergency operation, this symptom is not always as indicative of crisis as it appears. Blood in the peritoneal cavity always suggests peritonitis, and hence, many ectopic pregnancies still go undiagnosed prior to operation. In Dr. Grier's report the percentage of cases showing abdominal wall rigidity is also high.

While posterior colpotomy is not always essential to diagnosis, yet it is a valuable procedure in doubtful cases and even in those in which there is little or no doubt,

it is worth while because in a certain proportion of such cases the situation can be handled entirely from below. The presence of infection in association with a pelvic hematocele must also be constantly held in mind. The phrase "tubal abortion," which is still used so freely, does not impress him as meaning very much. He believed that cases of this sort are invariably implantations at the abdominal ostium. It is difficult for him to believe that a gestation sac implantation higher up can be disgorged and extruded. Such a thing may happen but he has seen no cases that would justify the correct use of the term.

DR. ROBERT T. FRANK, New York City, by invitation, presented a paper entitled, **Three Phases of Gynecologic Plastic Surgery.** (For original article see page 172.)

#### DISCUSSION

DR. JOSEPH L. BAER asked how and when the satchel handle flap was changed from skin outside to skin inside and the dimensions of the original flap. He called attention to a method of closing a vesicovaginal fistula of small size in which the scarred orifice is disregarded but a circular flap of vaginal mucosa is dissected loose around the fistula and this flap is inverted into the bladder lumen through the fistula. The bladder wall is then sutured externally with a purse-string and the vaginal mucosa sutured separately. He wished to emphasize the value of the LeFort operation for prolapse in elderly women with a small uterus and relaxed abdominal walls. For elderly women with atrophic uteri and good abdominal wall, the Murphy extra fascial fixation is ideal. The Watkins-Schauta interposition operation is well adapted for the ordinary case of prolapse with cystocele in which the bulk of the uterine corpus is sufficient to serve as a plug in the hernia of the anterior fascia. This was used in 41 per cent of 212 cases of prolapse operated upon by the gynecologic staff of the Michael Reese Hospital.

DR. HENRY SCHMITZ described a case in a patient who was engaged to be married but had an absence of the vagina, and he constructed a vagina for this patient according to the Davis method. The patient was very carefully followed up; dilatation was maintained with a set of graduated rectal dilators which the patient was instructed to use at home until the time of marriage. Since then he has examined the patient several times, and he is amazed at the elasticity, width, and depth of the new organ.

The advantage of this operation over the Frank operation is that it can be executed at one sitting.

DR. N. SPROAT HEANEY said that he had quite a few patients present themselves for the making of an artificial vagina but until recently he felt that Baldwin's operation gave the best results. He always painted the picture as he saw it to the patients with a result that none cared to submit to this procedure. A year ago he had a young lady present herself who had a very long labia minora which made it possible for him to perform Grave's operation using the labia minora as flaps of which to make the walls of the vagina. The case was very successful. This operation is preferable to the one described by Dr. Frank providing the labia minora are of sufficient length to promise enough flap tissue for the construction of the vagina. So often, however, the labia minora are tiny and inconsequential in which event the operation described by Dr. Frank undoubtedly would produce gratifying results.

DR. CAREY CULBERTSON said that Dr. Frank's procedure for vesicovaginal fistulas brings out the fact that the free mobilization of the bladder wall so that the fistulous tract may be closed without tension, is a thing of fundamental im-

portance. That was taught by Kelly years ago. For these fistulas Dr. Culbertson prefers to use an anterior colporrhaphy incision which enables as extensive mobilization of the bladder as may be necessary or even desired. Where a postoperative fistula is inaccessible one might have to open the abdomen in order to free the bladder and close the fistulous tract from above. This procedure, however, is not as easy as described by Leguen and in his experience is seldom necessary.

He was interested to note Dr. Frank's success with transposition of the uterus and that it is his procedure for correction of cystocele instead of an operation for procidentia uteri. This is exactly its application as Dr. Watkins employed it. Dr. Culbertson prefers to limit the operation to cases in which the uterus does not come out of the vagina and where the organ is suitable in size and normal in function, that is not subjected to metrorrhagia. In his experience it has most excellent results for cystocele and urinary incontinence.

Dr. Frank's unsatisfactory results in the use of the LeFort operation he regretted. This has been a very satisfactory procedure indeed in the few patients in which he has employed it. In elderly women, those between sixty-five and seventy-five years, he has found it most satisfactory in ten or twelve cases. It is simple, speedy, superficial, relatively free from hemorrhage, and not causing shock. It retains the uterus well and also serves admirably to hold up the bladder and prevent urinary incontinence.

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## NEW YORK OBSTETRICAL SOCIETY

MEETING OF DECEMBER 11, 1928

DR. D. P. MURPHY, of Philadelphia, read by invitation a paper on **The Outcome of 625 Pregnancies in Women Subjected to Pelvic Radium or Roentgen Irradiation.** (For original article see page 179.)

### DISCUSSION

DR. G. FAILLA, of the Radium Research Laboratory, Memorial Hospital, New York City, discussed the question of dosage in connection with these effects. We have a certain amount of radiation used in the vagina or uterus in the case of radium, or externally if x-rays are used. Of this radiation, a certain fraction only reaches the ovaries, but the ovaries are very sensitive to radiation, and this fraction is sufficient, in some cases, to cause sterility, either temporary or permanent.

Now, as to whether any effects are caused by radiation depends on the dose which reaches the ovaries. In using x-rays for diagnostic purposes the amount of radiation used is very small, it is only a flash, and even if it is a case of fluoroscopy it may last a few seconds or minutes, but in any case the amount of radiation which reaches the ovaries is very small and the sensitivity of the ovaries is not sufficient for us to fear complications from that source, but when radiation is used therapeutically, then complications may be expected.

In considering the sensitivity of the ovaries it might be well to examine, for instance, workers in x-ray departments and in radium laboratories. There it is found that the girls employed as technicians usually show blood changes before any menstrual disturbances are observed. If the blood does not show definite changes due to radiation, it seems safe to assume that the ovaries have not been injured.

Dr. Failla felt that it is always dangerous to irradiate a pregnant woman. Dr. Murphy's statistics may be questionable or some errors may have crept in, but we know little about the effects of x-rays on future generations. A good many people have been burned and have had cancer develop in the x-ray burns, something

which was not suspected twenty or twenty-five years ago, and we do not know what may develop twenty or twenty-five years from now from radiation which may be considered perfectly harmless today. Therefore, the use of x-rays and radium should be limited as much as possible to the conditions which are definitely known to be benefited by such procedure.

The experiments with animals which Dr. Murphy is carrying out may throw considerable light on this question. Already some experiments have been made in which future generations of mice or flies have been affected by radiation, and some of the abnormalities have been transmitted through a great many generations. Dr. Bagg has done work of that sort at the Memorial Hospital, and he has mice now which show abnormalities in their young a great many generations after the first pair that they radiated. Dr. Muller has definitely established that by means of radiation abnormalities can be produced which are transmitted from generation to generation according to definite laws in genetics.

DR. I. C. RUBIN said he was struck with the low percentage of stillbirths in the 74 cases that were irradiated during pregnancy. At Mount Sinai Hospital (N. Y.) in cases where abortion is therapeutically indicated and massive castration doses of x-ray used, a series of some 50 or more cases has proved that the pregnancy does not proceed in the vast majority, that abortion actually takes place, so that at least in the early months of gestation, irradiation is certainly lethal to the fetus.

DR. WILLIAM P. HEALY was especially interested in the preconception statistics and the diagnoses for which radiation had been used. There were 288 cases. Ten per cent (27) of them were carcinoma of the cervix. There were over 100 cases of so-called myopathic uterine bleeding. The dosage in the majority of those malignant cases probably was very small. It probably was intrauterine. There may have been some roentgen-ray therapy. The next table showed that despite the large number of pathologic uterine conditions which had been treated by irradiation, out of the number of pregnancies which actually occurred, there were comparatively few abortions in proportion to the number of full-term pregnancies. That is entirely contrary to the experience at the Memorial Hospital of New York. In other words, we are dealing in the very beginning with diseased uteri because they come with symptoms; they present pathologic conditions which require treatment, and these are the cases in which we have diseased endometrium, and as a result we have abortions, we have abnormal pregnancies. Dr. Healy's experience has been that as a rule, these patients do not go to term, if they conceive at all. A very small number of conceptions was noted in the cases of nonmalignant disease of the uterus that have been treated by radiation therapy at the Memorial Hospital, and only a comparatively insignificant number has reached term. They have all aborted or had a premature labor of a fetus that did not survive, and that is in a sense what one would expect those cases to do, regardless of whether they had or had not been treated by radiation therapy. They represent diseased uteri.

DR. HIRAM N. VINEBERG considered that it would be just as essential to curet the uterus before roentgen-ray radiation as before the use of radium.

DR. MURPHY (closing) said that, regarding the influence of diagnostic roentgen irradiation during pregnancy, he could report concerning a woman who received a large series of photographic exposures in the pelvic region, for the diagnosis of possible stone in the ureter. The ureters were catheterized on two different occasions. Later she was found to have been pregnant about five weeks at the time the pictures were taken. She delivered herself at term of a child described as a cross between a "Mongolian idiot and a cretin." In view of the relatively high

frequency of microcephaly after *therapeutic* pelvic irradiation, the case just cited, suggests, at least, that the irradiation, diagnostic in amount, may have accounted for the disturbance observed in this child. This is the only instance which had come to Dr. Murphy's knowledge concerning defective children born after diagnostic roentgen irradiation.

Dr. Matthews spoke of the matter of dosage. A study of roentgen dosage was very difficult to make, since information on this point was lacking, at least as regarded any uniformity with respect to technic. The radium dosages, on the other hand were recorded in a sufficiently uniform manner to make them suitable material for satisfactory analysis, which will be made in a later publication.

With regard to the statistical aspect of this paper: The figures reported upon were not well controlled, since it was impossible to secure any statistics concerning women with the same diseases who bore children and who did not receive pelvic irradiation. Also the definition of the term unhealthy child, being as broad as it was, added to the difficulty. In spite of the incompleteness of these figures, they at least represent the largest group of such case reports available for study.

Regarding the time of the irradiation during pregnancy, as it might influence the health of the subsequent child: Two cases have been studied in which the pelvic irradiation took place as late as the sixth month, followed by the birth of microcephalic children.

## BROOKLYN GYNECOLOGICAL SOCIETY

STATED MEETING, APRIL 5, 1929

DR. CHARLES A. GORDON, reported a case of **Massive Perirenal Myxosarcoma**.

This patient, aged thirty-five, single, admitted to St. Catherine's Hospital on February 7, 1929, was seen in consultation with Dr. Bruno.

For about a year she had noticed increasing enlargement of the abdomen, and complained of its weight, and of dyspnea upon exertion.

Menstruation normal, last period had occurred three weeks before. There had never been any pain, bleedings or discharge and there were no symptoms referable to the urinary tract. Her history was otherwise negative.

She was a healthy looking, well-built woman weighing 175 pounds, with negative heart and lungs, normal temperature, pulse 100, and respirations 24. Her blood pressure was 120/90, and her blood count showed 75 per cent hemoglobin with 4,300,000 R.B.C., 9,800 W.B.C., 70 per cent polymorphonuclear cells and 30 per cent lymphocytes. Her sedimentation time was seventy-two minutes, and the urine negative.

The abdomen was large, appearing like a pregnancy at term. A firm mass tensely cystic in spots filled the entire abdomen, widely distending both flanks, and touching the ensiform. Tympany could be found only far back in the right flank. The presence of fluid was doubtful but it was thought to be present, and a preoperative diagnosis of ovarian cyst was made, although rectal examination, made because of a vaginal introitus, was negative.

Operation was done two days after admission under gas-oxygen-ethylene-CO<sub>2</sub> anesthesia. The time of operation was two hours and thirty minutes.

Incision from ensiform to symphysis revealed a large tumor, filling the entire cavity, packing the pelvic fossae, and pressing upon the diaphragm. A tiny uterus with a few small fibroids was seen, and tubes and ovaries were normal. Stomach and intestine large or small could not be seen, and the posterior parietal peritoneum

covering the tumor was found in actual contact with the anterior abdominal wall everywhere. After longitudinal incision of its peritoneal covering, the tumor, with the left kidney, was removed with difficulty by shelling out dissection. The pancreas was lifted from its bed, almost removed with the tumor, and returned



Fig. 1.—Perirenal myxosarcoma showing lobulation, large veins and imbedded left kidney.

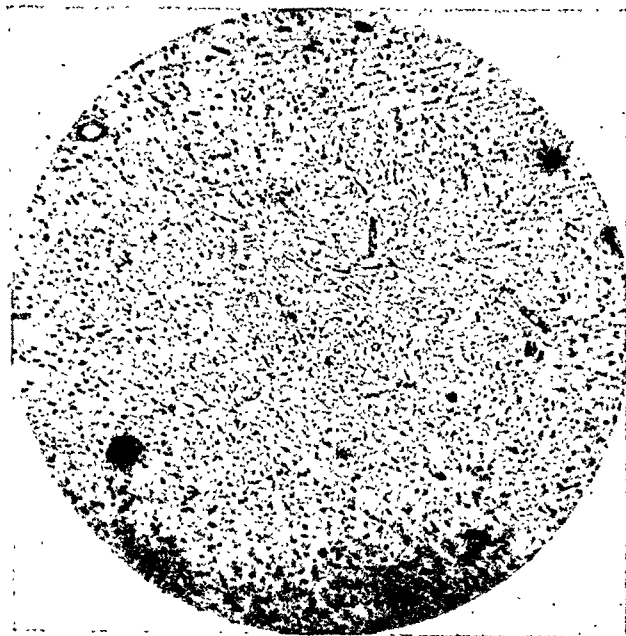


Fig. 2.—Section of perirenal myxosarcoma stained in hematoxylin and eosin. Low power. Magnification 100 diameters. Large number of myxoma and spindle cells. Stroma very acellular in spots.

to the abdomen after partial ligation of the splenic vein. At this time the right kidney and ureter were seen, and the stomach and flat coils of the intestine were found in the upper abdomen. After suture of the posterior parietal peritoneum, the abdomen was closed with fine chromic catgut with dermal silk for the skin.

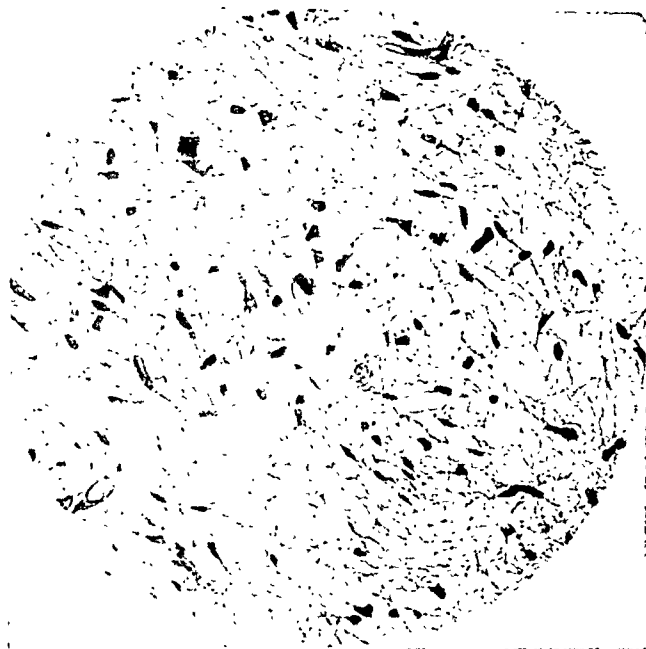


Fig. 3.—Area from Fig. 2. Magnification 250 diameters. Typical spindle and star-shaped cells with long processes. Matrix abundant. Myxoma.

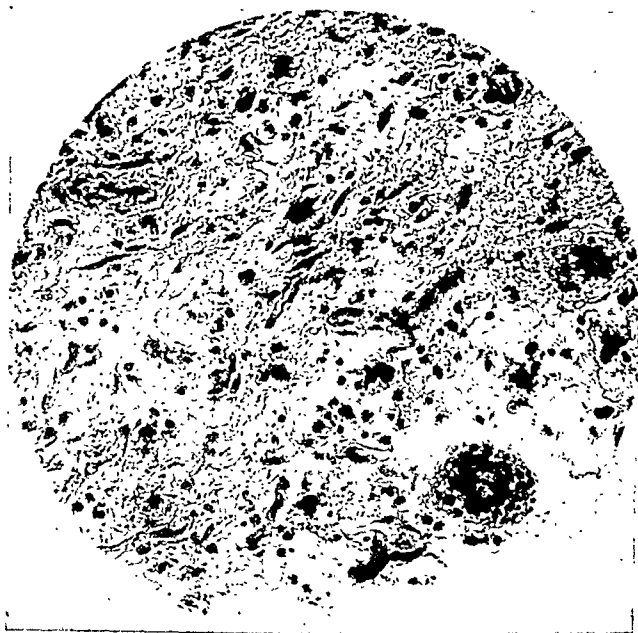


Fig. 4.—Area from Fig. 2. Magnification 250 diameters. Atypical cells with hyperchromatic nuclei, giant cells. Greater vascularity. Blood vessels containing tumor cells. Intercellular stroma of mucoid tissue.

The immediate postoperative condition was poor. Shock was successfully combated with CO<sub>2</sub> inhalation, morphine and glucose by hypodermoclysis. Two uranalyses ten and twelve hours after operation showed a large amount of sugar. Blood sugar four days later was 100 mg. per 100 c.c. of blood, and repeated uranalyses were normal. Convalescence thereafter was uneventful with the high-

est temperature 101.4° on the third day. The wound healed by first intention, better approximation of the redundant skin being secured by skin clips which were put in on the seventh day.

The patient's hospital stay totaled three weeks when she was discharged apparently well, weighing 120 pounds. She has since received deep x-ray therapy.

The tumor was examined by Dr. E. H. Nidish, and slides were seen by Dr. James Ewing.

*Pathologic Report.*—The tumor measured 46 cm. by 38 cm. by 16 cm. It weighed 36½ pounds or 16.5 kg. It was ovoid in shape, irregularly lobulated, with large veins coursing over its surface. It was gray in color, with some fat adherent, and roughly encapsulated in a thin but tough membrane which was absent in spots. On section it was translucent and gelatinous, with large blood vessels. Densely adherent posterior, eccentrically at the middle and outer thirds of the mass, was the left kidney with its upper pole normal and its lower pole irregularly quadrilateral in shape, thin and flat, firmly adherent to the mass with its vessels flattened widely over the tumor.

Histologic examination showed spindle, round and irregularly star-shaped cells with long processes disappearing in the matrix which was fibrillated and finely granular. Spindle, and giant cells with hyperchromatic nuclei were indefinitely arranged, often crowded about the blood vessels, but comparatively few in number, and varying much in size. Section from the kidney showed normal structure.

Dr. James Ewing to whom slides were submitted said "the tumor is a myxosarcoma and is probably derived from the perirenal fat tissue. The tissue contains comparatively few cells and a great deal of mucoid stroma. Yet the cells are quite atypical and hyperchromatic, and I think the tumor is moderately radioresistant, very likely to recur, and may produce pulmonary metastases."

#### DISCUSSION

DR. J. O. POLAK said that about fifteen years ago he had seen a tumor of the same type, the only one in thirty-five years, which involved the right kidney.

Dr. Polak found these myxosarcomatous tumors nonmalignant. Many of them do show sarcomatous change. His patient was seen from time to time during the last ten or twelve years, and there has been no recurrence. Dr. Polak emphasized the fact that in handling these tumors, if one splits the anterior peritoneal layer and is not too vigorous, it is surprising the ease with which they can be eviscerated. From the time one eviscerates the tumor, it is remarkable the ease with which they can be brought down to their pedicle and the bleeding controlled.

DR. CHARLES A. GORDON read a paper on the **Puerperal Morbidity Without Disinfection of the Vagina.** (For original article, see page 245.)

#### DISCUSSION

DR. H. W. MAYES said that during the last eighteen months at the Methodist-Episcopal Hospital, there were delivered 2,946 patients, exclusive of cesarean section, and only one mother was lost from puerperal sepsis, in an easy spontaneous delivery following a short labor. This gives a mortality rate from puerperal infection of 0.33 per 1,000 births. There were 6 other maternal deaths, making a mortality rate of 2.4 per 1,000 births. Four of these patients lived less than twenty-two hours following delivery, and died from shock or from hemorrhage; one was a chronic nephritic and died from toxemia, and the other died from influenza-pneumonia which she had when admitted to the hospital.



The uncorrected morbidity for the last 2,782 cases was 5.2 per cent. During the year 1928 we had 1,978 deliveries with a morbidity of 5.1 per cent and a corrected morbidity of 3.5 per cent. There were 4 maternal deaths for the year, giving a rate of 2.07 per 1,000 births.

The mercurochrome technic has been used at the Methodist-Episcopal Hospital on 7,724 patients with a morbidity of 7.8 per cent. The morbidity in 2,072 patients before the use of mercurochrome was 12.3 per cent. The only way we can judge of the value of any antiseptic or any technic is to compare it with what was done before trying the new. If Dr. Gordon has a morbidity at his hospital of between 3 and 4 per cent now, it would be much less if he used mercurochrome.

DR. H. B. MATTHEWS called attention to the fact that Dr. Gordon's statistics show that if you let the vagina severely alone and allow nature to take its course, so to speak, and effect delivery by a minimum amount of trauma, you may expect a low morbidity rate. On the other hand, the work that Dr. Mayes has done shows that the same care, plus a germicidal agent in the vagina, gives as low, but not any lower, morbidity. Apparently there is no definite conclusion to be drawn except in the method of delivery. Certainly the less intravaginal, intra-cervical, and intrauterine manipulation one does the less infection and less morbidity. However, with the mercurochrome instillations in the vagina, following exactly the technic used at the Methodist-Episcopal Hospital, namely, instillation must be done forty-five to fifty to sixty minutes before any delivery and every 12 hours while in labor it is likely that you can do more manipulation and have less morbidity than if you do not use a germicidal agent.

DR. PAUL TITUS, of Pittsburgh, Pa., read, by invitation, a paper entitled **Report of Investigations to Determine the Therapeutic Dose of Dextrose (d-Glucose) Administered Intravenously.** (For original article see page 208.)

#### DISCUSSION

DR. J. O. POLAK said that Dr. Titus had defended for years the use of dextrose without insulin, successfully, and with the study he has now shown us he has conclusively demonstrated that the pancreas is able under proper stimulation to do just what insulin in Thalhimer's hands has done.

DR. S. A. WOLFE said that with the sudden drop in blood sugar, the question arises, whether this fall from the standpoint of physiology and metabolism, does not represent an increased synthesis of the liver thus removing glucose and temporarily storing it as glycogen. The muscles, too, have similar glycogen storage properties, under this advanced glycemia. Dr. Wolfe believed that if the drop is due to increased insulin production, it would be necessary to show by the calorimeter that there has been an increased oxygen consumption during the administration of the glucose. Otherwise, the possibility of storage in the liver and muscles for subsequent oxidation must still be entertained.

DR. A. C. BECK asked how soon one may repeat the 75 gm. that are to be given in an hour and a half, and how often they can be repeated in the course of twenty-four hours.

DR. TITUS, replying to Dr. Gordon's question, said that dextrose may be administered in several different ways; by proctoclysis, subpectorally, intraperitoneally, and intravenously. By the latter method the rate of injection, and the dosage of the dextrose is more accurately controllable than by any other route. It may be of interest to comment that the local sloughs which occasionally follow the hypo-

dermic use of dextrose solutions are due, not to the irritation of the drug itself, but rather to its being given so rapidly, so that a pressure necrosis occurs.

Dr. Welton has mentioned the use of the terms "dextrose" and "glucose." Since the tenth revision of the United States Pharmacopeia it has been ruled that in speaking therapeutically of what was formerly called glucose we must use the term dextrose, thus indicating the purified product whereas that which is now to be known as glucose is merely the commercial preparation for other than therapeutic use.

The point which Dr. Wolfe has made is an important one. It is probable as he has suggested that some of the disappearance of sugar from the blood as shown by the drop in the graphs is due to simple metabolism and storage of sugar. It would be difficult to concede that such a rapid disappearance as that which others as well as they have shown, could be due entirely to storage. That this rapid removal of injected sugar when the dosage is prolonged to the point of being excessive, is due to pancreatic response in the production of insulin is best proved by the fact that the blood sugar levels continue to fall below the original levels even to the point of producing hypoglycemic symptoms. Surely this must be due to something more actively aggressive than simple utilization or storage by the body.

Dr. Duncan, of Montreal, has suggested that some of the reactions attributed to faulty technic in the injection of dextrose solutions, were very likely hypoglycemic reactions from overdosage. It was this suggestion which focused attention again on the splendid work of Thalhimer along these lines. This attempt to establish the safe limit of the dosage of dextrose was a logical outgrowth of these ideas, all based on the assumption that endogenous insulin production is responsible for a large part of this disappearance of sugar from the blood.

Replying to Dr. Beck's question, this dose may be given as often as four times in twenty-four hours if necessary and repeated daily as required. Dr. Titus had done this on a number of occasions but found that it is seldom necessary to give very many doses of dextrose. In hyperemesis, for example, it is frequently the experience that one or two injections in one day or possibly on two successive days are all that is needed to clear up the trouble.

# Department of Reviews and Abstracts

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CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

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## Selected Abstracts

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### Sex of the Fetus

Sugiura, K.: Sex of Fetus in Japan. *Japanese J. Obst. & Gynec.* 12: 56, 1929.

The opinion generally held in Europe is that the male birth rate decreases gradually as civilization increases. In Japan, civilization has made rapid progress in the past fifty years but there has been no tendency for the male birth rate to decrease. Likewise the notion that the proportion of males is higher in the country than in the cities does not obtain in Japan for the reverse is true. In Japan the excess of males among the live births does not differ much from that found in Europe, but in Japan the excess of males among stillbirth is much lower than in Europe. In Japan the excess of male over female births is lower among the illegitimate than among the married women. A certain relationship exists between the season of the year and the sex of children, but there is no relationship between temperature and excess of male births.

J. P. GREENHILL.

Wetterdal, P.: Two Questions Pertaining to the Sex-Ratio in Newly-Born Infants. *Acta Obst. et Gynec. Scandinav.* 6: 59, 1927.

It has often been shown that in abortions the number of males is far greater than that of female fetuses. No one has as yet determined this ratio for premature infants, hence the author undertook this study. From a study of 80,000 deliveries, he found that the ratio of males is almost continuously diminished from the thirty-second week of pregnancy when it is 138.2 to the forty-sixth week when it is only 95.6. Contrary to the opinion of others the author could not find any difference in the sex-ratio in primiparas and multiparas nor did the sex-ratio have any relationship to the number of pregnancies the women had.

J. P. GREENHILL.

Blumenfeld: Time of Coitus and the Sex of the Child. *Deutsche med. Wchnschr.* 51: 108, 1925.

Siegel studied the relation between the age of the ovum at the time of intercourse and the sex of the resulting child, and found that postmenstrual intercourse resulted in 86 per cent of the children being males, while intercourse from fifteen to twenty-two days after the beginning of menstruation resulted in 86 per cent of the children being females. He considers that ovulation occurs from ten to fifteen days after menstruation and therefore, according to his investigation the older or, as he says, the riper the egg, the bigger the chance of producing a male.

The author made a similar study of 46 children resulting from postmenstrual intercourse, of which twenty were males and twenty-six females. He believes that

Siegel's theory may not be sound because it is a known fact that spermatozoa may live in the uterus and tubes for eight days or more so it is not possible to tell how long after intercourse the ovum becomes fertilized.

F. A. PEMBERTON.

Crew, F. A. E.: *The Relation of the Sex of Offspring to the Time of Coitus During the Oestrous Cycle.* British M. J. 2: 917, 1927.

Recent work has revealed considerable evidence to show that sex-reversal of the egg before fertilization does occur in certain forms. The subject is of such interest that it was thought to be desirable to undertake further experimentation. The albino rat was chosen as experimental material; six males from one and the same litter were used, and 100 females, which all belonged to the same strain as the males, being all related and line bred.

The conclusions arrived at from this study—concerned, it is true, with numbers that are much too meager to be of any real significance—are entirely negative. It must be remembered that it is well-nigh impossible for any investigator to conduct experimentation on a sufficiently large scale, and that it is therefore desirable that experiments of this kind should be multiplied so that out of a considerable series adequate data may be secured. So far as they go, the present figures tend to support the contention that the time of service in relation to the estrous cycle is a factor of no importance in the matter of the determination of sex in the mammal.

In an experiment, designed to determine the sex ratios resulting from coitus during the first three hours and during the last three hours of estrus respectively in the rat, no difference was noted between these two groups.

PROSHEK.

Bleyer, L.: *Researches With the Lüttge-v. Mertz Alcohol Substratum Reaction and the Interferometer Method After P. Hirsch for the Serologic Determination of Pregnancy and the Determination of Fetal Sex.* Schweiz. med. Wehschr. 56: 498, 1926.

The Abderhalden method for the determination of pregnancy is discussed together with its difficulties. Similar methods were used by various men in the attempt to diagnose early cases of carcinoma, tuberculosis, and endocrine disturbances with no certain results. Several men using these methods tabulate results of fetal sex determination and pregnancy with varying success of from 60 to 80 per cent of positive results. The author employing the alcohol substratum reaction, following it in detail with the greatest care, concludes that there is no difference between the use of powdered organ and serum. He tried out the various methods suggested at the present time, and in the case of the serum of 71 pregnant patients taken between the eighth and tenth months with the alcohol substratum reaction he found 50 per cent who gave a positive pregnancy reaction and 55 per cent who gave a correct sex determination. He raises the question as to whether the failure of more positive diagnoses of pregnancy could not be due to the fact that perhaps the placenta reaction was not so apparent or satisfactory in the last weeks of pregnancy as in the first weeks, and he was of necessity compelled to use serum for late pregnancies. In using 42 sera from pregnancies of the last month and employing the interferometer method of P. Hirsch, 50 per cent were positive for pregnancy but 70 per cent were correct for sex determination. The value of the test unquestionably lies in the fact that with a positive result the patient certainly is pregnant while a negative may not be necessarily accurate.

A. C. WILLIAMSON.

**Vogt, E.:** *The Hormonal Influence on Sex in Animal Experimentation*. Med. Klin. 24: 207. 1928.

During pregnancy hormonal substances pass from mother to fetus and vice versa. Vogt experimentally produced sterility in rabbits by the injection of insulin. He also found that these injections affected the female sex cells so that the sex ratio after the subsidence of the sterility was changed. The offspring was almost entirely female and the author is of the opinion that insulin changed the affinity of the female sex cell for spermatozoa in such a way that only those spermatozoa were attracted which would give rise to females. Fellner obtained the same results by experimentally injecting feminin, the female sex hormone, into rabbits. The hormone was obtained in fairly pure form from the placenta, and it was found to possess the same antidiabetic properties as insulin. These experiments indicate that there is no definite specificity of hormones as was formerly thought and furthermore, that there is a close relationship between hormones and vitamins especially between the ovarian hormone and vitamin E. Vogt's experiments also confirm the rule that animals which give birth to a number of young at one time, produce essentially females in time of distress. The author believes this is necessary for the propagation of the species because one male can fertilize many females.

J. P. GREENHILL.

**Dyroff, R.:** *Interferometric Predetermination of Sex in 100 Cases*. Monatschr. f. Geburtsh. u. Gynäk. 73: 129, 1926.

The Abderhalden reaction and its modifications, such as the Lüttge-v. Mertz reaction, are not better than the best of the optical methods, namely, the interferometer. The principle of the latter is as follows: Serum from the patient to be examined is mixed with an organ extract (testis or ovary) and kept in an incubator. If the organ extract is affected there is an increase in concentration of the serum. The latter can be measured by comparing it with the original serum. Of the 100 cases examined the sex was correctly determined before birth in 74.

J. P. GREENHILL.

**Patti, F.:** *An Intradermal Reaction for the Diagnosis of Fetal Sex*. Arch. di Ostet. e Ginec. 13: 1, 1926.

Because it has been found that a male fetus produces certain symptoms in the mother, i.e., hyperpigmentation and vomiting, it was deduced that some substance passes from the male fetus into the blood of the mother. It is further believed that this substance is elaborated in the testis.

Many methods have been devised for detecting this substance in the maternal blood (methods of Abderhalden, Lehmann, Manoiloff, Gurewitsch). Patti uses a modification of Lehmann's method, injecting intradermally both the extracts of the male and female sex glands. He injects the extract of the testis in one area with a control beside it and in another area the extract of the ovary.

After the injection there is a latent period of twelve to fourteen hours. At that time in case of positive reaction there is a reddening, infiltration and edema of the area, two to three centimeters in diameter. This area is slightly tender upon pressure and the skin is somewhat hot. The reaction is practically gone on the third or fourth day, but a small area of pigmentation may remain for fifteen to twenty days.

From observations made on 34 patients the author draws the following conclusions:

The reaction is constantly positive in the normal pregnancy with male fetus. In the case of a female fetus the results are quite variable. In five cases of pathologic pregnancy with an albuminuria the reaction failed completely. It was also negative in one case of fetal monstrosity and in one case of dead fetus in utero. In one case where the pregnancy was complicated by typhoid fever the result was negative.

In general the results show that in a physiologic pregnancy a diagnosis of sex can be made quite consistently after the seventh month and even within twelve hours postpartum.

The amount of glandular extract injected is not stated.

E. L. FAUST.

## Correspondence

### On the Synergism of Magnesium Sulphate and Morphine\*

*To the Editor.*—The use of magnesium sulphate as a synergist (and not merely an addition) has been clearly and definitely established clinically. The clinical test is the final and the only essential one for practicing physicians. An analysis of the first classical case† in which the potentiation of morphine was established beyond all reasonable doubt is in order.

Morphine in water alone was given twice with a total elapsed time	
for the suppression of pain	5½ hours
Average time for suppression of pain	2 "
Morphine in magnesium sulphate was given to the same patient seven	
times with a total elapsed time for the suppression of pain	94¾ "
Average time for the suppression of pain	13 "

Here is an increase of over 500 per cent in value of morphine by the addition of an amount of magnesium sulphate (2 c.c. of a 25 per cent solution of the salt) that when used alone is insufficient to suppress pain. Pain was seemingly suppressed for nineteen hours in this same patient by 3 c.c. of magnesium sulphate alone, but this was *subsequent* to the previous injection of morphine and magnesium sulphate, and we have a right to conclude that a hang-over resulted. This seems to be proved by the fact that the next hypodermic of magnesium sulphate alone, 3 c.c. of a 25 per cent solution, there was severe pain after three hours, as by this time all the morphine had disappeared from the system. This one clinical case alone would be worthless as evidence, but we have 84 cases from two widely separated hospitals having no connection with each other, to confirm and continue the comparison.

From the Presbyterian Hospital, New York City. (First series of cases)	
14 surgical cases given morphine and water, average time for suppression of pain	4 hours
16 surgical cases given morphine and magnesium sulphate, average time for suppression of pain	16 hours
An increase in value of 300 per cent.	

The series of cases from the Presbyterian Hospital was given 400 c.c. of a 4 per cent solution of magnesium sulphate (4 drams or 240 grains of the salt).

\* A reply to an article by Beckman, Harry. "The alleged synergism of magnesium sulphate and morphine. AM. J. OBST. & GYN. 15: 1, January, 1928.

† J. A. M. A. 85: 1482, November 7, 1925.

This 4 drams (240 grains) might possibly be interpreted as additive and not synergistic, but Smythe (*Am. J. Surg.*, July, 1923 and *Memphis Med. Monthly*, 1922) after using this technic for some time stated that "continued use of a 25 per cent solution in a large number of cases enables me to report that the analgesic effect of morphine is prolonged with equal certainty and success by a smaller dosage. We now rely upon 3 small doses of morphine, one-eighth grain each; with the second dose of morphine is added one-fiftieth of a grain of atropine; each dose is dissolved in 2 c.c. of a 25 per cent solution of magnesium sulphate." The following are the results obtained:

From the service of Dr. Frank D. Smythe (deceased), Memphis, Tenn.

27 surgical cases given morphine and water, average time  
for suppression of pain 4 hours

27 surgical cases given morphine and magnesium sulphate,  
average time for suppression of pain 15 hours

An increase in value of over 250 per cent.

Things which are equal to the same thing are equal to each other. While 240 grains of the salt might be considered sedative, 24 grains cannot. 6 c.c. of a 25 per cent solution of magnesium sulphate alone given previous to an operation will not quiet pain at all after an operation. Three-eighths of a grain of morphine given in divided dosage in water previous to an operation will quiet pain for four hours after an operation. Three-eighths of a grain of morphine given in divided doses in 6 c.c. of a 25 per cent solution of magnesium sulphate will quiet pain for four times as long, or from fifteen to sixteen hours, an increase in value of from 250 to 300 per cent. *This is definite synergism.* Smythe states that "40 per cent of the patients thus prepared did not require an analgesic *at all* after operation. The appetite returned earlier because of the absence of pain and restlessness incident to the trauma inflicted at operation. Less nitrous oxide is required and a higher percentage of oxygen can be used than in cases where the morphine is given in sterile water. Fifty per cent of the cases required no ether. The patient is neither frightened nor apprehensive concerning the operation or its outcome. The stage of induction is greatly shortened and there is rarely a period of excitement." In spite of these many advantages of the synergistic method, Carl Henry Davis\* of Milwaukee states, in referring to obstetric analgesia, that "pharmacologists question the value of adding the magnesium sulphate, and the carefully controlled animal experiments of Beckman indicate that it is better to omit it." Beckman's animal experiments from a clinical standpoint are worthless inasmuch as he did not use the magnesium sulphate as it is used clinically.

That Beckman does not understand the synergism of magnesium sulphate and morphine is shown by his statement, that "the presence of the magnesium sulphate did not enable smaller doses of morphine to overcome the pain." Neither I nor any one else has ever hinted at any time that "smaller doses" of morphine could be used "to overcome pain" in the presence of magnesium sulphate in any amount. What I said was "it seems to act mechanically with morphine holding it in contact with the tissues longer than morphine alone is able to maintain such contact." Hence, the *same amount* of morphine must be used with magnesium sulphate as with sterile water. I have distinctly stated that one-eighth of morphine is not converted into one-sixth, or one-sixth into one-fourth, or one-fourth into one-half.

Beckman further states that issue can be taken with his work only, when "it can be shown that *exactly similar investigations* have been made with entirely different results." I refuse to do this as his experiments are worthless as to either

\*AM. J. OBST. & GYN. 15: No. 6. 807-808 Dec., 1927.

proving or disproving the prolonged effect of morphine when magnesium sulphate is used instead of plain water. No further animal experiments are necessary as any physician can prove the synergism of magnesium sulphate with morphine by alternating the synergist with water as was done in the first case reported in this letter. Other obstetricians who have used magnesium sulphate in obstetric analgesia state that they do not get within 50 per cent of the practical results when the magnesium sulphate is omitted.

I disagree with Beckman when he states that the synergism of magnesium sulphate with ether and novocain has no bearing upon the subject.

As magnesium sulphate does potentiate the value of these drugs it is reasonable to see if it potentiates other drugs, and all such experiments have a bearing upon the synergism of the magnesium ion with morphine. It has been proved by Barbour and Winter\* that "combinations of amidopyrin with magnesium chlorid in experimental animals exhibit antipyretic synergism and, to a lesser extent, diminished toxicity." Also, "magnesium salts in mice appear to reduce the toxicity of salicylates (protective antagonism). Magnesium augments the antipyretic action of sodium salicylate and of aspirin. When given subcutaneously with salicylate to fevered rabbits, the earlier stages of antipyresis are characterized by marked synergism." The synergism of magnesium sulphate with morphine and novocain is life saving with laboratory animals when ether vapor is used as the anesthetic. The experiments of Gwathmey and Hooper† prove this conclusively. Four healthy albino rats were employed for each experiment. Two of the animals were given intramuscularly magnesium sulphate, novocain and morphine. Two animals served as controls and were not given anything. These animals were given the drugs as we use it clinically, i.e., before the anesthetic is given. The controls died from within eight to ten minutes. The synergised animals survived the anesthetic from twenty to twenty-five minutes. This shows an increase in value as regards life of 150 per cent. Magnesium sulphate is put up in ampoules either alone, or with morphine, or with morphine and 2½ per cent novocain. If the practitioner prefers he can sterilize and make his own magnesium sulphate according to the formula of Dr. John Auer as follows: Weigh out 250 gm. and add enough water to make 1000 c.c., thus making a 25 per cent solution. A *chemically pure* magnesium sulphate must be used. (Reference: *Anesthesia*, Gwathmey, ed. 2, p. 650).

There is no more danger in administering morphine in 2 c.c. of a 25 per cent solution, as far as life is concerned, than there is in administering the morphine in 2 c.c. of water. We know this because in using it in over 10,000 cases of obstetric analgesia at the Lying-In Hospital, New York City, stillbirths have not increased.

Before accepting modifications and suggestions, it might be well for the obstetrician to thoroughly familiarize himself with the *results* of the standard technic and *then* omit the magnesium sulphate for comparison. Copies of the technic as it is being used at the Lying-In Hospital, 200 to 300 times each month will be sent on request to that institution. If it can be proved that by omitting the magnesium sulphate or anything else better results can be obtained, the suggestion will be adopted.

My conclusions are presented as follows:

1. The synergism of magnesium sulphate and morphine has been definitely proved clinically, both in obstetrics and surgery, increasing the value of morphine 250 per cent to 500 per cent.

2. Experimentally, this synergism is life saving with laboratory animals, when ether vapor is used as the anesthetic. Clinically, it is also life saving, decreasing

\*Proc. Soc. Exper. Biol. & Med. 25: No. 7. 582, 587, April, 1928.

†J. Lab. & Clin. Med. 10: No. 8, May, 1925, and Interstate Post Graduate Med. Assn. North America, Oct. 12, 1925, p. 92.



both morbidity and mortality. It should be used with *all* methods of anesthesia and analgesia. Carefully kept synergistic obstetric analgesia records of nearly 20,000 cases show that it is far superior to "twilight sleep" in every way.

3. The synergism of magnesium chlorid with amidopyrin, sodium salicylate and aspirin has been proved in the laboratory by Barbour and Winter, and has an indirect bearing upon the subject under discussion.

4. The synergism of magnesium sulphate and ether has been proved for the albino rat, rabbit, dog, and man, and is of practical importance in relation to the synergism of magnesium sulphate and morphine.

5. The probability is that magnesium sulphate synergises with almost any drug with which it is compatible, either by prolonging its action, deepening its effect, reducing fever, or in other ways.

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## Books Received

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L'ACCOUCHEUR MODERNE. *Precis obstétrique.* Par Adrien Metzger, chef de clinique chirurgicale à la faculté de médecine de Paris. Avec dessins originaux. Paris, Librairie Felix Alcan, 1928.

DIE FRAU. Ein neuzeitliches Gesundheitsbuch. Mit 70 Abbildungen. Von Dr. med. Hermann Paull in Karlsruhe. Verlegt von Strecker und Schroeder in Stuttgart, 1929.

DIE KRITISCHEN JAHRE DER FRAU. Von Dr. med. G. Boekh in Stuttgart. Verlegt von Strecker und Schroeder in Stuttgart, 1928.

PATHOLOGY OF THE ACUTE RESPIRATORY DISEASES AND OF GAS GANGRENE. Medical Department of the U. S. Army in the World War. Vol. xii. Washington, U. S. Government Printing Office, 1929.

GYNECOLOGY. A textbook of the diseases of women. By Lynn Lyle Fulkerson, instructor in obstetrics and gynecology, Cornell University Medical School, etc., etc. With 612 illustrations, three in color. Philadelphia, P. Blakiston's Son & Co., 1929.

GONORRHEA AND KINDRED AFFECTIONS. By George Robertson Livermore, professor of urology, medical department of the University of Tennessee, Memphis, Tenn., and Edward Armin Schumann, associate professor of obstetrics, University of Pennsylvania, etc. D. Appleton and Company, New York, 1929.

PHYSIOLOGIE GYNÉCOLOGIQUE, et Médecine des Femmes. Par Henry Vignes, accoucheur des Hôpitaux de Paris. Masson et Cie, éditeurs. Paris, 1929.

METHODS AND PROBLEMS OF MEDICAL EDUCATION. (Twelfth Series.) The Rockefeller Foundation. New York, 1929.

STUDIES IN THE PSYCHOLOGY OF SEX. Volume VII. Eonism and Other Supplementary Studies. By Havelock Ellis. Philadelphia, F. A. Davis Company, 1928.

# The American Journal of Obstetrics and Gynecology

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## Original Communications

### PRESIDENTIAL ADDRESS

#### SOME LITERARY DOCTORS OF MEDICINE\*

BY C. JEFF MILLER, M.D., NEW ORLEANS, LA.

THE evolution of American gynecology, as more than one writer has pointed out, may be traced in the addresses of the presidents of the American Gynecological Society. Through the years, from the days of Fordyce Barker and the founding of the Society, the present has been considered in them, the past reviewed, and the future painted, until in 1921, in one of the most brilliant medical addresses ever delivered in America, Chipman of Montreal gave us the whole subject in epitome. So I shall not endeavor to do again what has been so ably done before me. On the other hand, my choice of subject is limited by my own limitations. I cannot present to you, as other presidents have done, new discoveries in the laboratory, new methods of diagnosis, new operative procedures. I am that step-child of modern medicine, a mere clinician, translated to a special field, if you will, but still a clinician.

I propose, therefore, to speak to you today from this chair which has been honored by the men who have preceded me in this office and which I now occupy by your gracious mandate, on a subject only remotely connected with medicine. Sampson, you will remember, devoted practically the whole of his presidential address in 1922 to a consideration of the value of hobbies for all men, and chiefly for physicians. Well, my hobby has always been what physicians have achieved when they turned to follow what Goldsmith, I think, called "the draggle-tailed muses," and with your permission I shall pass by the science and art of gynecology and obstetrics, and speak to you today on one phase of that theme.

\*Read at the Fifty-fourth Annual Meeting of the American Gynecological Society, Old Point Comfort, Va., May 20, 1929.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

Since the time of Greek medicine, there have been physicians as eminent in literature as they were in their profession, and from the time of Thomas Linaere, English medicine and literature have likewise often joined hands. Linaere was physician to Henry VIII, to Wolsey, Colet, Warham, Box, More, Erasmus, Lily, and a host of other famous men. He ranked high among the doctors of his own day, and he has come down to posterity as the founder of that noble organization, the Royal College of Surgeons. But literature was his love, and he gave up his rich practice and took Orders, not that he felt a vocation but that he might devote himself to the revival of learning in England. As Osler says, he sought to restore to English medicine the uncorrupted spirit of Greece, and even a cursory survey of his work shows how well he succeeded in his self-imposed task.

We need not seek for writing of real merit only in the field of pure literature. In this day Barrie's libel no longer holds, that the scientific man is the only man now writing who has something to say, and the only man who does not know how to say it. I deny that absolutely. We have many physicians who write with distinction on medical themes, whose literary achievements are quite as notable as their professional skill. I need mention only a few: Sir Berkeley Moynihan, who writes on even the most strictly medical subjects with lucidity and charm; Sir Humphrey Rolleston, who has clothed his physic with philosophy and wisdom; Sir Clifford Allbut, who at eighty-five produced *Greek Medicine in Rome*, a book as remarkable for its scholarship as for its contributions to medical history; Fielding H. Garrison, who has done notable work in the same field; Harvey Cushing, that brilliant surgeon and accomplished litterateur, who in all of his writings achieves the excellence we have come to expect of the author of *The Life of Osler*; finally Sir William Osler himself, Regius Professor of Medicine at Oxford, and Stephen Paget, son of the great Sir James.

I wish that Stephen Paget's *Confessio Medici* could be put into the hands of every young physician before he begins to practice, and I wish that he would read, mark, learn, and inwardly digest it. It is a picture of the medical profession at its highest and best, sprung from the priesthood, devoted to the succor of mankind, a calling, not a trade, whose rewards cannot be reckoned in gold and silver, and whose disciples are called to it as truly as St. Francis was called to follow his dear Lady Poverty. He is a wise man, this old physician, who tells us what he has learned, so far as he has gone, from his life, so far as it has gone, who knows the frailties of humanity and does not ignore them, but who points above them and beyond them to the ideals that can be striven for even though they be not wholly attained. This is a medical book, intended principally for medical men, but if it be not true literature also, then Apollo has blinded my eyes.

Gilbert Murray, the great classicist whom he succeeded as the President of the Classical Association of Great Britain, said of Sir William Osler that "he represents in a peculiar way the learned physician who was one of the marked characters of the seventeenth and eighteenth centuries, and he stands for a type of culture which the Classical Association does not wish to see die out of the world,—the culture of a man who, while devoting himself to his special science, keeps, nevertheless, a broad basis of interest in letters of all kinds." Osler has left medical papers of value on many subjects, and he wrote a textbook which is still the standard for all who have come after. Indeed, he touched nothing which he did not adorn. But his peculiar genius is best exhibited in his miscellaneous addresses, his occasional papers and his lay sermons. In his presidential address at Oxford, almost his last public utterance, on *The Old Humanities and the New Science*, he apologized for his small Latin and less Greek, but to us he seems extraordinarily well read in both, read in the truest sense, in that he absorbed their culture and bathed himself in their spirit. He went far beyond the *sine qua non* set down by Bagehot, that any writer of English, if he know not Latin and Greek, must at least have a strong conviction that both languages existed. In this special address Osler reveals himself as the true humanist, forever interested in the interests of humanity, as he strives to recall to the real values a war-torn world which has forgotten them, and as he pleads for that civilization which Hippocrates pictured, in which love of humanity, *philanthropia*, shall be joined with love of the craft, *philotechnia*, and thus wisdom, *philosophia*, shall be justified of her children.

Like Stephen Paget, Osler has his own philosophy. Equanimity, he taught, is the way of life, and work is its master word, and with these as guards one may "bear success with humility, affection of friends without pride, and be ready when the day of sorrow and grief comes to meet it with the courage befitting a man." How well that simple faith supported him we know when his own trial came, when his beloved and only son fell on the blood-stained fields of France, one of that company of gallant gentlemen who gave up their lives that mankind might live.

All of Osler's writings are "memorable speech." They are characterized by a lucid and beautiful style, a style which is illuminated by a sort of high clarity and which exhibits a most astonishing fecundity of quotation and allusion. Like Francis Bacon, he seems to have taken all knowledge for his province. His pages are strewn with inverted commas, but even more striking are his allusiveness, his indirect references and almost unconscious tags of speech, which show not the learning of a pedant but the intimacy of a lover. The story goes, you know, that two examinations can be set upon Osler, one on his pathology and

therapeutics, the other on his quotations and references, and that the latter is more difficult to pass.

C. MacLaurin and Joseph Collins represent a stream of tendencies in modern literature which, in spite of its brilliance, I cannot admire unqualifiedly. The former is an Australian surgeon who has written two quasi medical books entitled *Post-Mortem* and *Mere Mortals*, in which he analyzes the diseases of the great figures of literature and history. It is a Zola-esque performance which gives evidence of a vast amount of historical and general information, plus a very ingenious speculative ability, but for my own part, I could wish that the author had devoted his not inconsiderable talents to more worthy things. No doubt most of the characters whom he depicts were extremely unpleasant persons, but why dwell on men who were lusters and women who were harlots, and why, if hereditary syphilis is one's obsession, as it seems to be this author's, why not present the subject as a medical thesis rather than in a book presumably intended for lay consumption?

For the last several years Dr. Collins has been turning out books which purport to analyze, from the standpoint of a practicing neurologist, current tendencies in literature and life. Unfortunately he looks at both with an eye jaundiced by his own specialty, which invalidates, it seems to me, most of his reflections, for he utterly lacks that aspect of impartiality which Matthew Arnold declares to be the first requirement of the true critic. His recent performances, too, incline me to agree with the commentator who remarked that an excellent journalist was lost to the world when Dr. Collins took up medicine.

The medical men who have written their autobiographies have in no wise added to their reputations by these performances. T. A. Emmet and Marion Sims performed surpassing services to gynecology, Sir James Paget and S. D. Gross were great surgeons, Edward Trudeau revolutionized the treatment of tuberculosis, Wilfred Grenfell succored a people, David Livingstone began the civilization of a continent, yet, with the possible exception of Livingstone, their books, from a literary aspect, represent only a succession of missed opportunities, however interesting they may be from other standpoints.

The medical biographers of medical men have done their task rather better. Sir Rickman John Godlee, who wrote *The Life of Lord Lister*, was handicapped by two things, that he was Lister's nephew, which made him, we may assume, lean over backward in order to avoid the charge of bias, and that by Lister's own repeatedly expressed desire the book was to be a record of his work and not the story of his life. The result is that the human touch is entirely lacking and that the gloom in which Lister's life went out seems a veritable twilight of the gods.

Quite otherwise is the story of Sir James Mackenzie by R. MacNair Wilson. *The Beloved Physician* is the record of a life of simple good-

ness and unswerving devotion to duty. From the day that he was attracted to medicine by the colored lights that shone in a chemist's window, Mackenzie consecrated himself, you will note the word, to general practice, and during the course of that practice he taught the medical profession how to study disease and how to evaluate symptoms, and he became himself the world's leading authority on affections of the heart.

*The Life of Sir William Osler*, by Harvey Cushing, to my mind is one of the most extraordinary literary achievements of our day. That a book in two volumes and more than thirteen hundred pages can, in this age, hold the attention of the reader from start to finish is one marvel. That a biographer who knew his subject as intimately as Cushing did Osler, who stood in the affectionate relationship that he did to him, can keep himself entirely out of the picture, is another. And that, in a book that is of necessity crammed with medical detail, there can be drawn the likeness of such a radiant personality, the record of such gracious living, is the third. *The Life* is dedicated to medical students, with the hope that something of Osler's spirit may be conveyed to those of a generation that did not know him, and no one, I think, can read it without feeling how beautifully Cushing has wrought his labor of love and how adequately he has fulfilled his desire.

To turn to the fields of pure literature, there is no more interesting figure in them than Sir Thomas Browne, the seventeenth century physician who practiced medicine for a profession and wrote his books as a recreation. His life, though not quite the miracle he himself makes it out to be, is really rather extraordinary. After his university days and his travels abroad, he married a lady "so perfect that they seemed to come together by a kind of magnetism," who bore him ten children and with whom he spent forty happy years. The storms of Civil War raged about him but he remained undisturbed in his country seat. A king lost his throne, a king lost his head, but Sir Thomas "caught the opportunity to write of old things." The thunder of battle was heard afar off, while he concerned himself with thoughts of the hereafter, suggested by the finding of a funeral urn, and speculated as to why elephants have no joints and why storks live only in free states, and why America, being full of beasts of prey and other noxious animals, though by what passage they came over he knows not, should so strangely lack that most necessary creature, the horse.

*The Religio Medici* was written to defend himself and his professional brethren from the ancient imputation of irreligion, and, as was the way in that informal age, was published without his knowledge and in several unauthorized editions before his own version appeared in 1643. It had an extraordinary popularity in his day, a popularity which still continues among a most heterogeneous group of persons, though I know of none who, like Sir Kenelm Digby, found it necessary to read it

through in one night and forthwith write a criticism of it amounting to three-quarters of its length.

Its charm is twofold. Part of it is certainly due to the recollection of the serene, happy gentleman who, in the spirit, at least, never passed from the shadow of Oxford's dreaming spires. He lived his life, he tells us, shaking hands with delight, his conversation, like the sun's, with all men. He is so modest that he is quite willing to bring up the rear in heaven, so charitable that he can sympathize with all humanity, can endure all theological systems,—*mirabile dictu* in that age,—can admire his enemies, can feel a sort of compassion for the devil, and can picture in the hereafter a life of toleration where the damned would be released from their tortures and where one limbo would be reserved for the virtuous heathen. Indeed, he is happy enough to pity Caesar if he may have the things he asks of life, the peace of his conscience, the command of his affections, and the love of God and his dearest friends.

That is one aspect of the charm of Sir Thomas Browne. The other is his majestic style, scarcely equalled again in English literature, with its old-world Latinisms, its stately rhetoric, its mysticism and its humor, its pomp and circumstance, its noble rhythms, like the full stops of a cathedral organ or the ancient chants of a chapel choir.

MacLaurin, as might be expected, dismisses *The Religio* with the statement that it is a farrago of quackery, mysticism, credulity and astrology, written in gorgeous and unnecessarily obscure language. But one whose eyes were less blinded loved it above all books. To Sir William Osler it was next only to the Bible, and it went with him all the way, *comes viæ vitæque*, until finally it was clasped in his hand as he lay at rest in the shadow of the Lady Chapel near St. Frideswide's Watching Chamber, with the scarlet gown of Oxford about him and the peace that passes understanding on his face.

John Locke, the famous author of *The Essay on the Human Understanding*, the apostle of common sense in philosophy, was a physician and an excellent one. William James, though he never practiced, not only completed his medical course at Harvard but for many years taught physiology and comparative anatomy there, passing from those departments to psychology and thence to philosophy. If, as the critics say, his famous brother Henry is a novelist who writes like a psychologist, certainly William James is a psychologist who writes like a novelist. He raised the standard of intellectual honesty in America, he humanized philosophy, he helped many a doubting soul to feel a new glow of hope and courage, and I know of no writings, scientific or otherwise, which can be read with more of the pleasure one accords to true literature.

Havelock Ellis, the dubious parent of much of the present thought and social practice concerning sex, took a medical degree in order, apparently, that he might foreswear that career and become, in his own

words, a physician of souls. I confess that I am too much prejudiced against Dr. Ellis to evaluate his spiritual ministry, and I also confess to a most unchristian glee at his own acknowledgment in his latest book that in spite of his amiable intentions toward the world, he has not received from its people the cooperation he had the right to expect.

Decidedly more of the earth earthy is Samuel Smiles, who practiced medicine for two years until he found it more profitable to write *Self-Help, Thrift, Character*, and other predecessors of the accumulated successful lives now presented to the public in *The American Magazine*. He was the popular apostle of a sort of universal Jack Hornerism, a cheerful optimist who headed a school that believed in the equable distribution of life's prizes, and, judging from his early record, he undoubtedly did more good there than he could have done in medicine.

Erasmus Darwin, grandfather of the famous Charles, practiced medicine as his life work and practiced literature between visits, in the form of poetry and treatises on philosophy, botany and education. Charles Darwin, many of whose scientific generalizations his grandfather had anticipated, began to study medicine, but anatomy disgusted him, the operating theater horrified him, and materia medica brought to his mind only cold, breakfastless hours devoted to the properties of rhubarb. So he turned his attention to other things, and *The Origin of the Species* followed in due course. Thomas Henry Huxley began to study medicine because medicine was in the family, but the abstract sciences of biology, zoology and comparative anatomy soon claimed his interest. To the end of his life, however, he frequently appeared as lecturer before the College of Surgeons, and certainly the medical profession may lay some claim to this man who introduced a new school of biologic inquiry and whose whole performance, like William James's, lies in the realm of real literature.

John Arbuthnot, member of the Royal College of Surgeons, harveian orator, court physician, who helped Pope "through that long disease, his life," in his portrait of John Bull was the first to depict the English type, now flung to the Seven Seas. In Martin Scriblerus he has added an unforgettable portrait to the gallery of English humorous characters. He was, however, singularly careless of his literary reputation, for his witty writings were anonymous, his friends altered them as they chose, and his children made kites of his papers.

The first book I ever owned, if you will forgive the personal reminiscence, is still as dear to me as it is, I am sure, to many of you. I refer to *Rab and His Friends*, that charming volume of sketches written by Dr. John Brown of Edinburgh, the pupil and later the assistant of the famous Syme. The memoir of his father is as beautiful as any similar memoir in English literature, but it is not as touching as the sketch which gives the book its title. I know that none of you, if you have ever read it, can forget that hospital ward where the sweet old country-



woman lies dying, cradling in her empty arms the fancied form of the little child she had lost, watched by the faithful dog, nursed by her inarticulate, heavy-handed husband, whose touch to her was always gentle, and brooded over by the great surgeon, helpless to stay her dread disease.

In this same volume is that classic of childhood, *Marjorie Fleming*, the story of the wee wifie who was the devoted friend of Sir Walter Scott. She is revealed in her journals and letters, this little maid with her quaint philosophy and her bad spelling, her confession of her sins and her personal views of the devil, who made her behave so ill in God's most holy church, and who must have something to do with the multiplication she finds so difficult. How she lives, this child with her sweetness and her gayety, and how the old physician lives, too, in his tender comments and his loving interpretation of her short, beautiful life!

Medicine, says Sir Humphrey Rolleston, may be said to have refused the overtures of Oliver Goldsmith, and teaching, the law and the Church would have none of him either. Indeed, so the tale goes, the Bishop before whom he appeared for ordination stated very bluntly that a candidate who would clothe himself for such an occasion in scarlet breeches must be constitutionally unadapted to Holy Orders. Throughout his life, almost to its end, he continued his efforts at medicine, although the College of Surgeons rejected him and the naval boards declined to appoint him. On his last attempt at private practice he wrangled with the apothecary over the dosage, and the patient, quite wisely we cannot help feeling, sided with the latter; Goldsmith thereupon vowed never to practice again, in which resolution he was warmly applauded by Topham Beauclerc, who advised him, if he were resolved to kill, to concentrate on his enemies. Finally he precipitated his own end by an attempt to prescribe for himself, the fever potion being apparently, like Pet Marjorie's multiplication of seven times seven, what nature itself couldn't endure.

But if he failed in his efforts at the various professions, how well he succeeded when he fled to literature. Aside from his didactic poetry and familiar verse, he has left a series of essays which in real charm approach Charles Lamb's; a comedy, *She Stoops to Conquer*, which is still being acted before delighted audiences; and a novel, *The Vicar of Wakefield*, which contains the portrait of one of the best loved characters in English fiction. But he is no more beloved than is the simple, generous, loving, improvident man who created him, and who, if he did not adorn medicine, is one of the bright stars in the crown of English letters.

Like Goldsmith in many ways, though totally unlike him in the distinction he achieved in his profession, is Oliver Wendell Holmes. He began his general practice in Boston, with the motto that the smallest

fever would be thankfully received, and for thirty-five years he was professor of anatomy and physiology at Harvard, occupying, as he said, not a chair but a whole settee. He anticipated by twenty years the work of Semmelweis on the contagiousness of puerperal infection, though unfortunately he did not follow it to its logical conclusion. As a lecturer he was so successful that he was always assigned the last hour of the day, because at that time no one else on the faculty could keep the students awake. Brander Matthews suggests that his own description of Paré may well be applied to him, good, wise, quaint, chatty, shrewd. Certainly he was a gentleman and a scholar, a physician learned in the lore of his calling, a man of the world in the highest sense of the term, and, as Howells says, universally interesting because he was universally interested.

How, doing the work that he did, Holmes managed to write at all, let alone so much and so well, is the chief wonder of his literary career. He was in turn poet, essayist, and novelist, though his novels are simply medicopsychologic studies, conceived by a physician and composed by an essayist, and owing whatever merit they may possess to the flavor of Holmes' own personality.

It is as an essayist, however, that he is at his best. In *The Breakfast Table Series*, frankly modeled on the eighteenth century type, we have the author himself, a whimsical old humorist, looking at life through his professional spectacles, regarding the world and its people from all angles, but always with kindness and urbanity, never with acerbity and scorn, and talking about himself with a delight that is wholly contagious. He had always been, he said, good company for himself, and surely in these essays he reveals himself as delightful company for others.

S. Weir Mitchell, at fifty-three, when he was one of the world's leading neurologists, wrote his first novel, having been advised by Holmes, while he was still in his twenties, to hide literature in his desk until medicine were full grown. At that age, when medical success made long holidays possible and his natural inclination made idleness impossible, he turned to what, except for stern need, would have been his life work. We must, as Osler says, go to other centuries to find such a combination of a life devoted to the best interests of science with literature and social distinction. He wrought not with the haste of a journalist but with the deliberate leisure of a man of letters. He has a distinction of style possessed by few of our romancers, and though, like Holmes, he was too much of an essayist ever to find himself in dialogue, his historic backgrounds are unfailingly correct, and it is only because the physician has overshadowed the author that his literary fame is not greater. He knew as much of evil and sorrow as other men, indeed he knew more than most, but he always lived "in the sunshine

of life," and the tone of his books is a tonic in an age sick and weary with literary perverses.

Tobias Smollett, in the early eighteenth century, though he practiced most of his life, was never a successful physician. On the other hand, he ranks with Richardson and Fielding as a pioneer in the development of the novel form in English. Both in *Roderick Random* and in *Ferdinand Count Fathom* he makes use of his experiences as an apprentice in medicine and as a naval surgeon, presenting them with what he considers wholesome frankness but with what seem to us only brutality and ugliness. He was in a constant state of rebellion against life, and only toward the end does he begin to soften, so that his books, powerful and virile though they be, are not pleasant reading. Smollett did at least two things for the English novel: under the influence of the Spanish School he introduced the picaresque or rogue element, and in his painting of characters as types, with their superficial oddities of manner and speech emphasized, he profoundly influenced two of his greater successors, Sir Walter Scott and Charles Dickens.

Charles Lever, who was characteristically Irish in spite of a wholly English ancestry, with great difficulty obtained a degree from Trinity College, and was immediately appointed to various public offices, probably, it has been unkindly suggested, because cholera was epidemic and the medical boards could not be very particular. Even a fair practice failed to keep him in funds, and he turned to literature, pouring out, for the rest of his life, a succession of pot-boilers of which *Harry Lorrequer* and *Charles O'Malley* are probably the best known. It was his misfortune to be an author without a literary avocation, and it is characteristic of him that late in life he was made consul of Trieste by Lord Derby, on the ground that the office carried six hundred a year for doing nothing, and he was just the man to do it.

Sir Arthur Conan Doyle, before he turned to literature, did general practice and then ophthalmology. He had a waiting room, he says, but he found out very soon who did the waiting, and he thereupon decided that even though literature did not promise much, medicine seemed to promise less. Too little has been written about Conan Doyle as the author of historical novels, in which his best work has been done and in which his heart really lies, for it is as the creator of *Sherlock Holmes* that the world chiefly knows him. He cannot equal Poe in the invention of the macabre and horrible, he cannot equal Wilkie Collins in the portrayal of character, but he has none the less created a personage known to the whole world in the inspired detective with his disorderly room, his infinite and uncanny knowledge, his mouse-colored dressing-gown, his addiction to cocaine, his love of music, his consumption of shag tobacco, and his faithful friend Watson. One wonders how the practice of that particular physician must have fared with its constant interruptions, but we should be willing to take our chances with his

medical skill in order to hear more of his stories. It was a real stroke of genius which created him; the figure of Holmes has verisimilitude because he exists. With Watson, we fall on our knees. Like him, we expose our stupidity to permit the sun of Holmes' brilliance to shine. Like him, we stultify ourselves gladly that he may continue his deductions. Plain clothed detectives owe Sir Arthur no thanks, for he has created in the minds of the public an illusion of their ability quite impossible of attainment. Indeed, he himself had the curious experience, when he was in Egypt at the time of the Soudan Campaign, of finding that his *Sherlock Holmes* had been translated into Arabic and issued to local police as a handy and reliable manual of conduct.

Since the War Sir Arthur has turned his attention to spiritualism, thereby adding, as Huxley once said, fresh terrors to death. I admit that in his revelations of the hereafter he speaks with the authority of thirty years of honest investigation, but for my own part I prefer him as the creator of the decidedly earthy Holmes and his *fidus Achates* Watson rather than as the interpreter of the heavenly kingdom.

Time does not permit more than a passing mention of the group of physician-novelists who are writing today. It includes Henry Rowland, H. de Vere Stacpole, Somerset Maugham, Warwick Deeping, and Francis Brett Young. Warwick Deeping was in active practice when a successful first novel, *Uther and Igraine*, warranted his turning to literature as a profession. During the War, however, he returned to medicine, serving in the Medical Corps both in the East and in France. More than twenty novels were behind him when in *Sorrel and Son*, a vital and beautiful study of the devotion of a father to his more than motherless child, he struck a new note which he has continued in all his later books.

Somerset Maugham's first novel, *Liza of Lambeth*, is a piece of stark realism based on his experiences as house physician at St. Thomas' Hospital, on the edge of the London slums. *Of Human Bondage*, his most ambitious work, is practically an autobiography, and its fidelity to life and its gallery of living portraits, many of them reminiscent of his brief medical career, make it one of the outstanding novels of our age. Whether, as critics have declared, it belongs in the class with *Tom Jones* and *Pendennis* is a matter of personal opinion, but its worth cannot be denied. Mr. Maugham is equally as successful as a dramatist, his plays ranging from drawing-room comedies to the powerful if unpleasant *Rain*. One wonders, however, why, having shown what he could do, he saw fit to write or his publishers saw fit to issue his latest effort, *Ashden or the British Agent*. If he is attempting to assume the mantle which Conan Doyle seems to have laid down, most respectfully do we inform him that his shoulders are not fitted to bear it.

Finally there is Francis Brett Young, to my mind the most promising of the whole group. Because he was the son of a doctor he studied

medicine, and because his literary career seemed to promise little he continued to practice until he was invalided home from the War. His first two books had the unique distinction of being rejected by thirty-two publishers each. His first accepted books had excellent reviews and no sales, chiefly because they did not fit the mood of a world mad with the lust of war. Now, however, he is publishing novels of real distinction, and the long neglect of the critics has meant that he has been free to work out his own salvation because he has not had to submit himself to their importunities. His early South African stories have atmosphere, *The Young Physician* has realism, *The Dark Tower* is a study in shadows, but *Love is Enough* and *My Brother Jonathan* are pages of life. The figments of the first books have become living, sentient men and women, and the forge of life is making character. Mr. Young has a wholesome sanity of outlook in an age that in many of its literary fashions has gone quite mad, and he writes with a beauty of style and a precision of touch scarcely equalled in this generation of novelists. He is quite as happy in his background, and to me not the least charm of his books is his pictures of the English countryside, where the wild roses blow in the hedgerows, where the larks sing, where the hilltops melt into the clouds, a countryside whose sweet smells and sights and sounds are in contrast to the towns of the Black Country just beyond, with their stacks belching smoke and their furnace fires red against the sky.

They are an interesting group of men, these physicians and would-be physicians who have turned to literature for their recreation or for their life work. Many of them have been an honor to the profession, many of them have enriched the field of letters, a few have been equally distinguished in both callings. And I shall feel that I have not spoken to you today in vain if I can persuade you sometimes, when the cares of life weigh heavily upon you, those cares that are the inevitable lot of those of us who have chosen to follow medicine, to turn to the ripe wisdom of Stephen Paget and Sir William Osler, to the quaint tolerance of Sir Thomas Browne, to the wholesome sanity of William James, to the sweet gayety of Pet Marjorie, to the tender Vicar of Wakefield and the kindly old Autocrat, and to those more modern physicians who can help us to forget

“The lyf so short, the craft so long to lerne,”

and so who can give us fresh courage to bear the load.

NOTE: I am indebted to Dr. Pierce Butler, Dean of Newcomb College, for many helpful suggestions; to Miss Mary Louise Marshall, Librarian of the Orleans Parish Medical Library, and Mr. Robert Usher, Librarian of the Howard Memorial Library, for their assistance in procuring for me obscure references and out of print books; and to my secretary, Miss Elizabeth M. McPetridge, without whose assistance this paper could not have been written.

## MYCOTIC VULVOVAGINITIS

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THE case of mycotic vulvovaginitis here reported was encountered in a woman of thirty-five years of age, who first noticed the clinical symptoms of the disease at the beginning of the sixth month of pregnancy. The chief complaint at this time was the marked pruritus of the vulva and vagina, a burning sensation in the vagina, and some discharge. The symptoms were persistent and progressively disturbing, and the patient's husband, an obstetrician himself, began to worry and in order to settle the matter of diagnosis he brought to the laboratory swabs from the vagina. The following data covering physical examination were obtained:

Patient: primipara, last menstruation normal, January 1, 1928. Both family and personal history as far as the subject under discussion is concerned was practically negative. Menstrual periods began at the age of thirteen years and were always regular and without disturbing complications. During the first three months of pregnancy, nausea and vomiting were noted. About the early part of June, or at the beginning of the sixth month of pregnancy, the first signs of pruritus about the vulva were noticed. This began as a thin yellowish-white discharge, which at first caused little pruritus, but which was rather profuse in amount, requiring the wearing of a napkin constantly. Thin in the beginning, this discharge gradually changed in character, becoming more consistent, thicker and somewhat cheesy and granular in appearance. Careful examination of the vulva and vagina revealed the presence of irregularly distributed lumps of white, opaque, thick exudate. Gentle rubbing over the vagina with gauze was sufficient to remove these lumps of exudate, and after removal of the exudate no ulcerations or bleeding areas were noted, but the mucosa appeared markedly inflamed, red, and very painful on touch. The same, but less pronounced, pathology was found in the vulva.

*Laboratory Examination.*—On first examination, the vaginal exudate appeared strongly acid and smears showed budding vegetative forms of the yeast together with a long thick Gram-positive bacillus of the type of Döderlein's vaginal bacillus. The urine was slightly acid, but free of sugar. The efforts to identify the yeast yielded the following results:

In liquid media (nutrient broth) the organisms grew with the production of sediment and collar formation, but no pellicles were seen. No coagulation of litmus milk or gelatin liquefaction was noted. The gelatin stab growth had a rather typical inverted pine tree appearance produced by long, fine, hair-like mycelial extensions into the media along the line of stab. On Sabouraud slants, after four days, the growth appeared white, creamy, soft, elevated and with a clearly defined border. In the older cultures mycelial extensions beneath into the medium were observed but no aerial hyphae were found and no surface mycelium noted. A few of the tubes, after from eight to ten days of incubation, showed a very slight greenish tinge. Giant cell colonies were prepared with the Sabouraud medium in Petri dishes according to the technic of Mackie and after twelve days a whitish, opaque, moderate sized colony was grown. This was surrounded by thickened rounded edges and on

account of a central depression it looked like an inverted saucer. On potato the growth was not abundant and appeared dry and dull grayish-white with no visible villous extensions. The 0.2 per cent lactic acid-beer agar medium of Grace Hill was found to be of great value. The organism examined was killed by heat at 60° C. in fifteen minutes.

Fermentation tests were done, and, trying to avoid the confusion brought about by Castellani's over-faith in sugar fermentation as a dependable means of identification and classification of yeasts, we followed the conservative advice of Ashford and Mackie and used as key sugars only glucose, levulose, maltose, galactose, and saccharose. The organism in question attacked with acid and gas production glucose, levulose, and maltose, and acid was formed always in galactose and often in saccharose. These results were uniformly obtained by using Enlow's synthetic medium, broth sugar free medium and Hiss serum water medium. The organism was kept in Zweifel's solution of 0.5 per cent lactic acid for a week; when planted again on Sabouraud's medium it grew well and gave the same fermentation reactions.

Smears were stained with the Gram and Giemsa methods and with the supravital brilliant cresyl blue and Janus green-neutral red methods. Unstained preparations in the hanging drop and moist tissue culture-cell methods were also used. The organism appeared as bright, clear-cut yeast cells with a doubly refractive membrane measuring on the average 5 or 6 microns. It contained a well-defined nucleus and one or more vacuoles. Budding took place at or near the end of the cells, and actively growing cultures appeared rather pleomorphic as the result of the presence of smaller sized daughter cells, which on supravital staining took the dye avidly but did not show the inner structures as clearly as did the large mother cells. In the older cultures the vegetative forms had a much smaller nucleus, the cellular contour was sharper and a shell-like envelope was conspicuously seen. Septate mycelia were formed which continued to reproduce by budding only. The lateral and terminal conidia were present but no sporangia or ascospores. The articles of hyphae were straight, clear cut, bright and somewhat rounded and varied greatly in length, some being over 900 microns long. Budding took place near the extremity. These morphologic characters were best observed in moist tissue culture-cell preparations. The development of mycelia depended evidently upon the type of medium used. In fluid media, and especially in plain amniotic fluid obtained later from the patient, hyphae were formed very slowly and were composed of only two or three elongated cells while in the solid media of Sabouraud, and in blood with the addition of amniotic fluid, the mycelia were formed after thirty-six hours and as a rule grew outwardly, resembling in this way the growth of connective tissue explant in vitro. In dying cultures, thin, structureless, presumably sterile hyphae were prominent.

On the basis of the above described cultural, fermentation and morphologic features, the organism in question belongs to the class of fungi imperfecti, family of Oosporaceae, subclass of hyphales, and corresponds to *Monilia pilosis* Ashfordi or *Parasaccharomyces* of Andersoni.

It is needless to try to argue about the validity of the present classification of yeasts. The complicated and conflicting classification of Castellani is not shared by all mycologists. (Anderson, Ashford, Polacci and Nannizzi, Mackie and others.) The classification given by Mackie and Chitre in their splendid work on yeast and sprue published last August in the *Indian Medical Research Memoirs* appears to be simple and comprehensive and puts the organism we are dealing with into

the group of maltose fermenters, type *Monilia psilosis* Ashfordi, Class A pathogenic yeasts.

Cases of vulvovaginal thrush of English nomenclature, Soorkolpitis of German and Muguet vulvovaginal of French, reported in the literature are very few in number and only a small number of them have adequate bacteriologic data in regard to the exact type of the yeast found. Castellani's cases of mycotic infection of the vulva, vagina, and urethra are supplied with the best bacteriologic descriptions. This author since 1912 has carried out regular mycologic studies on every case of pruritus, vaginitis, and urethritis. Naturally, as the result of biochemical classification used the list of monilia he found appears unusually long.

It should be noted here that besides monilia groups I, III, IV and V of his ten-group classification he found also among his cases of vaginitis and pruritus of the vulvae *Cryptococcus*, *Epidermophyton cruris*, *Epidermophyton rubrum*, *oidium*, *aspergillus*, *sporotrichum*, *chladosporium*, *sterigmatocystitis*, *vibrio*thrix, and others. This variability of the yeasts found in both normal and diseased conditions of the vagina (Houlton, Salomon and Harris and Brown) may bring immediately the objection to attributing the pathologic manifestations described to the yeasts. Similar objections, based on the fact that from oral mucosa and the stool of normal individuals fungi were recovered in over 40 per cent, were raised against the pathologic relation of yeasts to sprue and bronchomycosis. However, leaving aside doubts regarding the etiologic importance of *Monilia psilosis* in sprue and pulmonary pathology, one still finds in the literature clinical observations and serologic investigations (Michel, Benedeck, Hines), as well as animal experiments with feeding and inoculation (Browne and Potter), that prove definitely the pathogenic and antigenic rôle of *M. psilosis*.

The physical symptoms of mycotic vulvovaginitis and the aspect of the mucosa vary greatly and depend on the case. The vagina, vulva, and skin of the genitocrural region may be affected. On the basis of type, location and pathologic manifestations of the lesion Prof. Le Blaye of Paris gives, in our opinion, the best clinical classification of mycotic vulvovaginitis. He describes the following eight clinical forms:

1. *Creamy vaginitis*.—This resembles in appearance the oral thrush and is manifested by the presence of white, opaque, thick exudate irregularly distributed in lumps which can be removed without difficulty from the mucosa and does not leave ulceration but shows a red and inflamed mucosa which is painful.

2. *Creamy vulvitis*.—The character of the mucosa is similar to that of creamy vaginitis but the redness, inflammation, and exudate are less pronounced. This form is usually associated with vaginitis and in case of abundant discharge the perineovulvar region may show intertrigenous or vesiculopustular form of inflammatory involvement.

3. *Ulcerative vulvitis*.—This is a severe form with superficial ulcerations, pain, lymphangitis, inguinal adenopathy, and occasional mycotic involvement of the bladder.



4. *Pseudoleucoplakic vulvitis*.—The mucosa appears whitish and opaque resembling leucoplakia. The curet removes with difficulty the whitish coat with superficial layer of the mucosa, but there is no accentuation in the wrinkling of the mucosa, papillomatosis or the true keratinization that are observed in leucoplakia and in lichenification.

5. *Exematiform vulvitis*.—Exudate is absent and the lesion is manifested by the formation of vesicular pustules which rupture and form small punctiform erosions. The inflammation sometimes extends into the perineum, genitoerural plica and may simulate intertrigo.

6. *Mycotic pruritus of vulvae or prurigenous mycotic vulvitis*.—In this form inflammatory manifestations may be wanting completely and only a few erosions due to scratching may be found. Leucorrhoea may give a similar picture. In this form parasitologic examination only can solve the matter of diagnosis. However, if one deals with long-standing pruritus that is not accompanied by lichenification, paleness and atrophy monilia infection should be considered.

7. *Vesiculopustular cutaneous form*.—This affects only the external teguments, the vesiculopustules are small, the vesicular stage is very short and cicatrization is rapid.

8. *Cutaneous intertrigineous examatous form*.—In the intertrigineous form the monilia can be found sometimes in the genitoerural plica but the vulva remains negative. Cutaneous involvement may extend into the pubis, anus, genitoerural plica, and even into the internal surface of the thigh.

In accordance with this classification our case reported here should be classified as type of exudative creamy vulvovaginitis and is doubtless of mycotic monilial origin.

*Treatment*.—On account of delay in diagnosis and the late stage of pregnancy our case presented from a therapeutic point of view quite a problem, especially during the last month.

In the beginning, for some time a 2 per cent solution of mercuriochrome was used and later 20 per cent argyrol. The relief obtained, however, was transient, giving ease from pruritus only for a few hours. In the standard textbooks of obstetrics and gynecology that were consulted, nothing definite could be found regarding methods of treatment of mycotic vaginitis in pregnancy, and especially in late pregnancy. In the long list of common antiseptic ointments and lotions prescribed by these textbooks for so-called pruritus we did not find any that would benefit our patient. Speaking of routinization and vagueness in treatment of the problem of vulvovaginal pruritus, one should be grateful to Doctors Greenhill, Davis and Colwell for splitting the big chapter on pruritus into subgroups of specific pruritus and also for giving a thorough clinicopathologic description and a systematic treatment of *Trichomonas vaginalis*.

Mycologic data on the development and growth of *Monilia psilosis* and our control studies in cultures and smears give every preference to Le Blaye's alkaline medication over routine antiseptic treatment. As soon as the treatment with 1 or 2 per cent bicarbonate of soda lotion followed by glycerine-starch-borate-soda bicarbonate suppositories (ovula) was instituted, the patient noticed a great relief and the symp-

toms of burning, itching, and abundant disturbing discharge rapidly subsided. At the same time the control vaginal smears showed disappearance of mycelial, virulent forms with increase in the number of a degraded type of yeast characterized by small nuclei and infrequent nucleation.\*

In order to avoid a possible infection of the vagina by the suppositories themselves, the latter were prepared with aseptic precautions and their bacterial content, which proved to be of harmless saprophytic nature, was checked up by both aerobic and anaerobic methods of culturing. This additional precaution permitted us to use this treatment up to the last week of pregnancy and with no trouble or complications whatsoever. Frequency of application of this suppository method was guided by subjective symptoms and bacteriologic examination and two or three treatments a week were sufficient to keep the patient free of complaint.

To our disappointment we were unable to get a Granugenol-Oil which Prof. Stephan uses with great success in the treatment of mycotic trichomonas and other forms of vaginitis in both pregnant and nonpregnant women. His observations and way of treatment are especially interesting since all of his ten Soorkolpitis cases treated were women of the second half of pregnancy. In his opinion the sublimate-borax-glycerin method is good for nonpregnant women where the speculum can be used and where cleaning with a 1 per cent sublimate solution, drying and subsequent rubbing with a 10 per cent borax-glycerin (or introduction of borax-glycerine capsules) can be applied. In pregnant women, however, on account of increased secretion and vulnerability of the vaginal epithelium this treatment is not sufficient. Granugenol-Oil favors the regeneration of the vaginal epithelium and for this reason it is superior to the borax-glycerin. In pregnant women Stephan uses the following procedure: Gentle cleaning by tampon with 1 per cent sublimate; drying and Granugenol-Oil application. After two or three applications of Granugenol-Oil the vaginal exudate acquires a granular appearance that easily may be taken for recurrence but on microscopic examination it is composed of epithelial detritus and regenerating epithelium. If this granular coat is removed a smooth glistening surface of regenerated healthy mucosa can be seen.

Before finishing our report we wish to point out a few essential and most important features of this case:

1. Vaginal yeasts in this case up to the time of delivery were accompanied by Döderlein's vaginal bacillus.
2. Mycelial forms appeared in the direct smears at the time when clinical symptoms were most severe.
3. The use of Le Blaye's alkaline-glycerin-sodium borate supposito-

\*While the investigation was under way a new case of mycotic vulvovaginitis was noted by one of us (F. F.). This new patient was in the seventh month of pregnancy and reacted most successfully to similar treatment applied.

ries improved the condition rapidly and always resulted in diminution of yeasts at the subsequent examination both in the direct smears and in the cultures.

4. The patient came to labor in good condition. Delivery was spontaneous and no postpartum complications were noted.

5. Amniotic fluid, evidently as the result of vaginal contamination, gave a growth of yeast and the amniotic fluid, *per se*, used as a medium, did not inhibit the growth of the yeast.

6. From the second day after delivery up to the present time (two months postpartum) yeast cells have not been found in the smears and cultures, the clinical symptoms have disappeared and the child did not show mycotic or any other infection.

Is this remarkable phenomenon of postpartum self-cleaning of the vagina brought about by Metchnikoff's phagocytosis with subepithelial macrophages? Is it the result of the combined action of amniotic fluid and some specific properties of the epithelium? Or, is the whole problem of postpartum cleaning solved by d'Herelle's bacteriophagic phenomenon? These questions still remain unanswered. Without a doubt, however, in addition to the above mentioned factors, the treatment used also played its beneficial rôle in the successful outcome of this case and materially relieved the symptoms during the last part of pregnancy.

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Gyllensvärd, N.. Two Cases of Absence of One of the Adnexa, *Acta obst. et gynec. Scandinav.* 7: 258, 1928.

When during a laparotomy one unexpectedly discovers that the adnexa on one side are missing, one may infer (1), that incomplete information was given concerning previous operations, or (2) that there is a malformation, or (3) that the absence is due to fetal or postfetal disease. In 1914 Ogorek collected 97 cases from the literature, and Gyllensvärd reports two additional cases. In the first case the adnexa had been completely absorbed after torsion and necrosis as indicated by scar tissue found in the left upper corner of the uterus. In the second case the author believes spontaneous amputation of the tube had taken place.

J. P. GREENHILL.

# THE MORPHOLOGY OF NORMAL MENSTRUAL BLOOD AND ITS DIAGNOSTIC VALUE\*

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CLINICALLY it is often of great importance to be able to differentiate definitely menstrual blood from other types of genital bleeding. In reviewing the work done on the cytology of menstrual blood, it was noted that certain uterine elements were found with a fair degree of regularity; furthermore it was thought that the observations on the vaginal cycle might have a practical value in helping to identify menstrual blood. With these facts in mind this investigation was undertaken in the hope that the correlation of the various factors above mentioned would enable us to differentiate menstrual blood from other types of hemorrhagic vaginal discharge and thus give us an additional diagnostic aid in pelvic diseases.

## RÉSUMÉ OF THE LITERATURE

Novak<sup>1</sup> states, "In addition to blood, menstrual discharge contains a greater or less amount of mucin, desquamated epithelial cells, bacteria and granular débris." Deirek recently has shown that there is cyclical activity of the vaginal mucosa characterized by desquamation and cornification in the premenstrual and menstrual phases. It was thought in view of these facts, that a morphologic study would enable us to differentiate menstrual blood from other types of vaginal hemorrhagic discharge.

Else v. der Leyen<sup>2</sup> studied the fragments of tissue found in the menstrual blood. She determined that during the menses pieces of mucosa containing glands and occasionally stroma resembling decidua, were extruded. The pieces varied from a few cells to centimeter-sized fragments. Her findings enabled her to establish the fact that in normal menstruation a definite amount of uterine mucosa was cast off. This question had been under discussion for many years and adherents for both the desquamation and nondesquamation theory were numerous.

Kate Linder<sup>3</sup> also obtained and studied fragments of tissue passed during the menstrual period. She, too, contended that desquamation of uterine tissue was a normal phenomenon and that in the pieces extruded both the compacta and spongy layers were included. She also determined that this mucosal desquamation ceased after the second day of the period. She described one peculiar fragment of tissue as made up of large, round cells of decidual-like structure, with a small nucleus and thick cell membrane, arranged in lamellae. In all probability in view of our results to be noted later on, this fragment was desquamated vaginal mucosa.

Sekiba<sup>4</sup> repeated the work of Kate Linder, examining fragments expelled during the menstrual period. He concluded that in the beginning of menstruation, mucosa in small macroscopic pieces is cast off. These fragments are rarely found after the first day and practically never on the third or fourth day. In some instances no pieces large enough to be examined macroscopically are passed, while

\*Read at a meeting of the New York Obstetrical Society, March 12, 1929.

in others huge fragments may be extruded. Microscopically this tissue can be identified as mucosa containing both stroma and glands. The cells show pyknotic nuclei and the entire fragments are infiltrated with leucocytes. He believes the entire compact layer and portions of the spongy layer are desquamated due to a necrotic process. The amount of desquamation varies in the individual.

Bohnen<sup>5</sup> studying uteri to determine the extent of the desquamation agrees with Schroeder that the mucosa both spongy and compacta is desquamated down to basalis. This process is practically completed by the second day.

Stickel and Zondek<sup>6</sup> investigated the menstrual blood from the hemologic point of view. They found a lower value for all the recognizable blood cells, both red blood cells, white blood cells and also for the hemoglobin. They noted that while there was a leucopenia, there was also a lymphocytic increase and polynuclear decrease. In the vagina the total blood cells were even less than the uterine blood. This phenomenon they accounted for by the fact that as the blood escaped from the cervix, small clots composed of red blood cells and leucocytes were extruded, which affected the total cell count.

Rotter<sup>7</sup> investigated the morphology of the menstrual blood with the object of utilizing his findings as a help in diagnosis. He studied the white cells and determined that in the menstrual blood there is always a decrease in the total count with a gradual polynuclear increase and a lymphocytic diminution. In the bleeding associated with inflammatory disease during the intermenstruum, the blood presented a leucocytosis and a lymphopenia. In fibromyoma with interval bleeding, the blood extruded had a cell count similar to the peripheral blood. In carcinoma the genital bleeding presented a leucopenia and lymphocytosis. He concluded from these findings that the examination of the genital blood might be of assistance in diagnosing carcinoma and the interval bleeding due to inflammatory diseases.

Heim,<sup>8</sup> in an exhaustive article on the growth of human tissue, found that mucosa obtained during the interval and premenstrual period, is viable. He was able to grow this menstrual mucosa outside of the body. The tiny fragments obtained in the menstrual blood he was unable to grow but he leaves the question open as to whether or not this same resistance to proliferation would exist if he were able to obtain larger sequestra. He points out that the mucosa obtained by curettage represented in all probability the small fragments that later would have been extruded.

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The present investigation was undertaken to determine the value of the histologic examination to differentiate normal menstrual blood from other bloody vaginal discharges.

One hundred specimens have been examined, some few in a complete series from the first to the last day of menstruation, others on one, two or three successive days and of others only one or two samples have been taken. In one case a complete series of a nine-day period was studied. To obtain the specimens a glass tube was inserted in the vagina, just within the introitus and fastened in place with adhesive tape. The women were kept in bed during the entire period. The blood collected was divided into 2 parts, one fixed while fresh in acetic acid 36 per cent, and one in 50 per cent alcohol. In some instances 10 to 20 c.c. were obtained, in a few hours; in others, only  $\frac{1}{2}$  to 1 c.c. which we found in most instances ample for our purpose. The material was centrifuged if necessary, imbedded in paraffin, cut and stained. Hematoxylin, eosin, van Gieson, and occasionally other stains were used. The constituents that were studied particularly were the vaginal and uterine epithelium, and to a lesser extent, other elements such as the leucocytes, both mononuclear and polynuclear.

The uterine epithelium was found in most marked profusion on the second day of the period. It occurred in 74 per cent of the cases. On the first day it occurred in only 50 per cent while on the third day 54 per cent. On subsequent days with one exception, it was not found. It occurs as small strips of columnar epithelium, at times consisting of only a few cells, well stained and as far as the histologic appearance can determine, viable (Figs. 1 and 2). At other times in long strands with many cells; some well stained, others showing degenerative changes. It occurred also as small groups of glands, sometimes only one tiny gland (Fig. 4A), in others in profusion with tortuous glands and surrounding stroma; while in several instances large masses similar to the tissue expelled in membranous dysmenorrhea were found (Fig. 3). In this latter type, no history of unusual pain was elicited. It would seem that with the first appearance of the menstrual flow uterine desquamation has already taken place, that it becomes more marked on the second day, diminishes on the third and ceases on the fourth day. This is the cycle in the usual four to five day type.

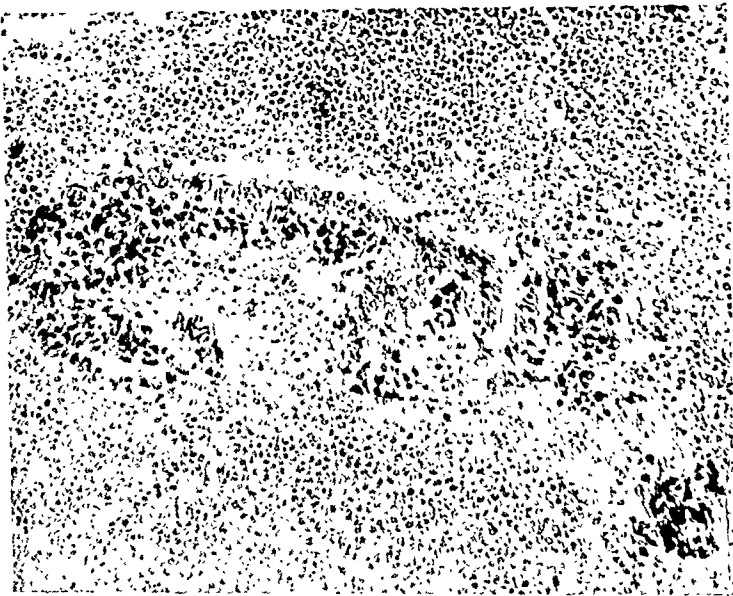


Fig. 1.—X 250. Strip of surface mucosa with small amount of underlying stroma and one small clump of stroma cells to be seen in the right lower corner. Sufficient for diagnosis of menstrual blood.

We also find stroma clumps which occur entirely independent of the epithelium and in varying profusion. They may occur as small clumps of darkly stained cells, oval, round or polygonal, varying from 5 to 20 cells (Fig. 4). The nuclei at times appear normal, well stained, at times showing pyknosis or other evidence of degenerative change. The stroma, however, does not show the same extent of necrosis as the epithelium, though in both cases the viable tissue (that is viable as judged by the histologic appearance) far exceeds the degenerative tissue in amount. The stroma extrusion too shows variations, being more common the second and third days on which days 90 to 91 per cent of the specimens contained stroma in varying amounts either free from or associated with epithelium (Fig. 4A). On the first day, 75 per cent of the specimens contained stroma, while on the fourth day, 50 per cent of the cases were still discharging stromal fragments. The presence of these fragments is extremely characteristic and constant, and though in some instances only one or two tiny clumps may be found, yet they enable one to state definitely that the fluid examined is menstrual blood.

We see a slight difference between the extrusion of the stroma and that of the epithelium. The stroma desquamation starts as does the epithelium on the first day, then diminishes on the fourth and fifth days. It is evident that the amount of desquamation varies in each individual case and may also vary at each period.

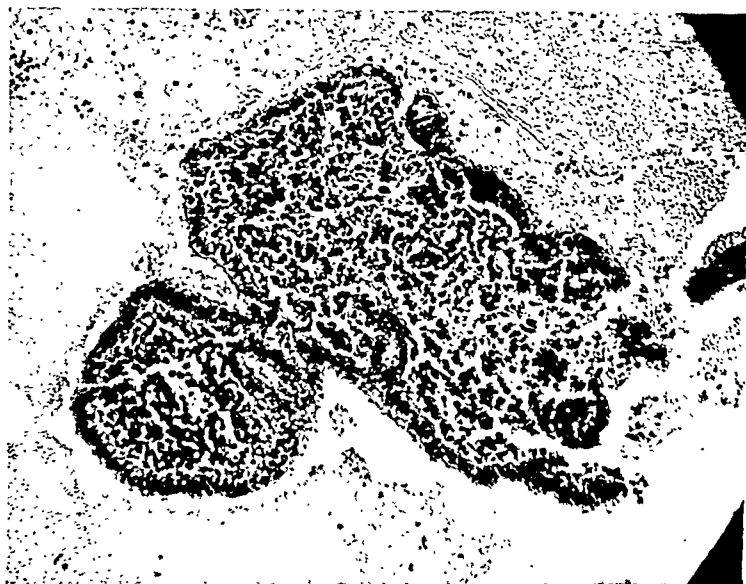


Fig. 2.—X 180. Large fragment of mucosa showing surface epithelium and a few glands, pyknosis of the nuclei; sufficient for diagnosis of menstrual blood.

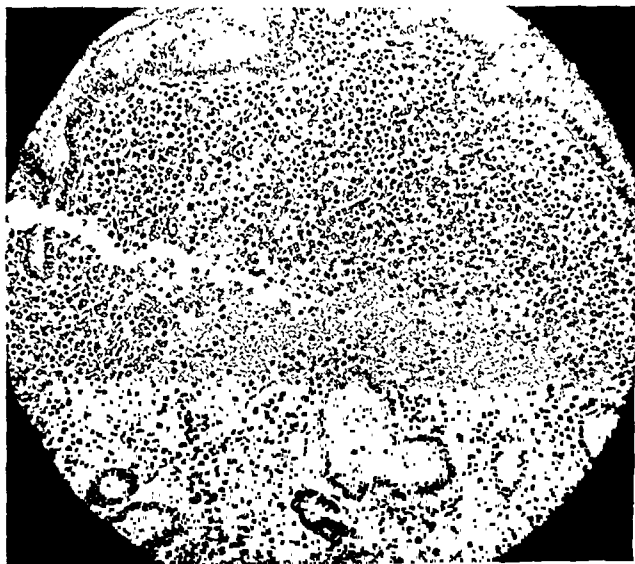


Fig. 3.—X 120. Large plaques of mucosa showing well preserved epithelium both on the surface and in the glands. Decidual reaction in the stroma. Resembles tissue expelled in dysmenorrhea.

This variability may account for the divergent views held by many authors as regards the amount and extent of the desquamation.

It is true that in a certain proportion of the cases (9 per cent) either uterine epithelium or stroma or both was missing. This of course might be due to the fact

that enough material was not examined or that in certain individuals this desquamation does not take place. Corner<sup>9</sup> has described in monkeys a periodic fundal bleeding not associated with ovulation, and not accompanied by the usual mucosal hypertrophy. It is possible that the absence of the mucosa in this small group of cases

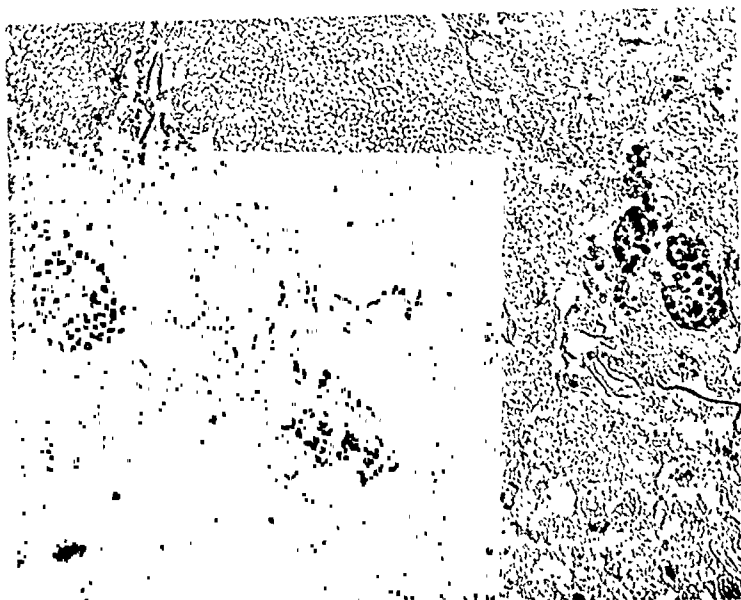


Fig. 4.—X 120. Small stroma clumps of well preserved cells at the right and left of picture; sufficient however to make diagnosis of menstrual blood. Vaginal spindles, broad and compressed, nonnucleated, present.



Fig. 4-A.—X 120. Uterine glands, well preserved, two small stroma clumps at lower portion of picture, sufficient to make diagnosis of menstrual blood.

may be explained also on a similar basis, namely, that in certain individuals menstruation takes place without mucosal desquamation, if not at every period, possibly at some of the otherwise normal cyclic hemorrhages. This question will be more fully studied later.

Another striking finding was the presence of desquamated vaginal epithelium.



It was difficult to establish a definite rhythm, as it appeared in practically every specimen of menstrual blood. We designated this epithelium as vaginal spindles if it appeared as isolated cells and as vaginal plaques when it occurred in sheets. In the first group, the cells occurred singly as either short flat spindles, containing a small round central nuclei, pale staining with a few taking a more intense stain, as large fat spindles with pale cell body and round central nucleus, or as long sinuous spindles with very faint staining, round or elongated nuclei or with no nuclei. These latter appearing as cell shadows (Fig. 5). This fat spindle had been described by Papanicolaou<sup>10</sup> in the vaginal spreads from pregnant women. Often about them were clumps of bacteria. The vaginal spindles occurred in 95 per cent of the cases on the first and second days; in 82 per cent of the cases on the third day and in 100 per cent of the cases on the fourth day. The individual number of cells varied, in some cases the spindles were numerous, occasionally the slides being covered with them, 50 to 100 in a field, and in other instances they were more scanty, sometimes one only or two to a field.

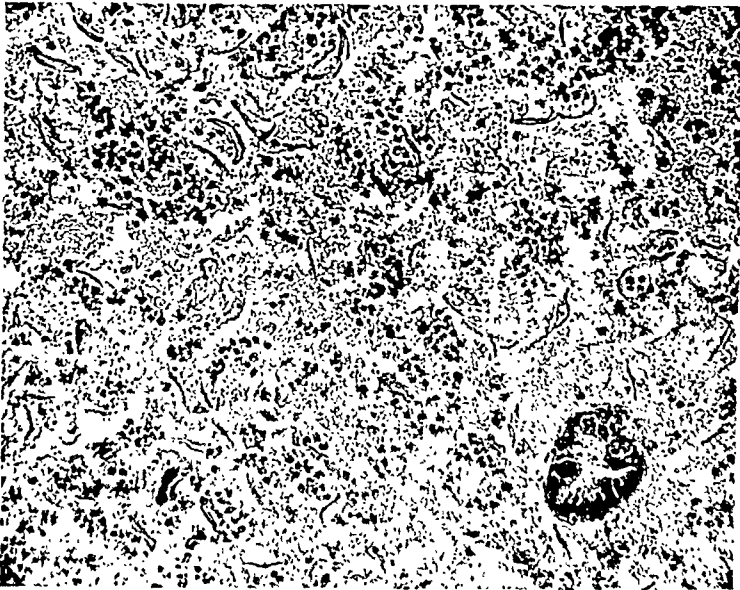


Fig. 5.—X 120. Mass of isolated spindle cells of varying types. Boat shaped, large and compressed, spindles and one small uterine gland well preserved in the lower right hand corner, sufficient to make diagnosis of menstrual blood.

The vaginal plaques varied likewise in their appearance. Three types were observed. In one the plaques were composed of layers of squamous epithelium, varying in number from three to four cells to masses of 100 or more (Fig. 6) and from three to four layers to ten or twenty. Here, too, as in the spindles, the cells are pale staining and apparently nonviable. The second type is represented by clumps or groups of large spheroidal or polygonal cells, probably the variation in the direction of the section making the difference in appearance. The nuclei in both groups are small, round, badly stained and central (Fig. 7). The third variety is seen as strands of cells two or more layers thick, crowded, nonnucleated for the most part; in many the cell markings are gone and these are just strands of cornified nonviable superficial epithelium (Fig. 8). The plaques are not as numerous as the cells of course, but are present in sufficient profusion to be easily found. On the first day, they occur in 50 per cent of the cases, rising on the second day to 72 per cent, dropping again to 55 per cent on the third day, and

to 25 per cent on the fourth day. Whether this cycle is dependent on a true endocrine impulse or is the result of the maceration of the menstrual blood, as yet cannot be determined.

Vaginal smears were studied with the assistance of Dr. A. A. Guttmacher to determine if any menstrual cycle could be identified but we were unable to definitely



Fig. 6.—X 150. Large fragments of vaginal mucosa. Well preserved cells. Such large fragments as these are uncommon.



Fig. 7.—X 200. Strips of cornified vaginal mucosa. One showing at its extremity to the right and below, a flat plaque of epithelium cut tangentially.

recognize any consistent rhythm in the cellular variation, except that it was noted that the vaginal desquamation in sheets occurred with fair regularity in the pre-menstrual phase, and during the period. The more detailed report will be given in a subsequent communication.

It may be stated, however, that no definite rhythm comparable to the cycle in

the rodent can be determined but it is a fact that as the menstrual period approaches, a more marked vaginal desquamation in the form of plaques takes place.

Deirek<sup>11</sup> and others have described in the vaginal mucosa a cyclic increase in the so-called functionalis with a desquamation of this layer just before and during the period. This would seem to be confirmed by the study of vaginal smears and menstrual blood. King,<sup>12</sup> in a careful study of normal women, states that there is a slight periodicity noted but not sufficient to lead to the conclusion that changes in the vaginal secretion serve as an index of periodic changes in the ovary or uterus.

A study of the white blood cells shows a striking finding. The number of polynuclear leucocytes varies tremendously. In the majority of the cases, they are fairly numerous in the vaginal menstrual blood, much more so than could be accounted for by the presence of the menstrual blood per se. In a preliminary study of the twenty cases where the leucocyte count of the circulating blood and of the menstrual blood as it escaped from the cervix, was undertaken, it was found that in all cases with a normal count in the peripheral blood, the white cell

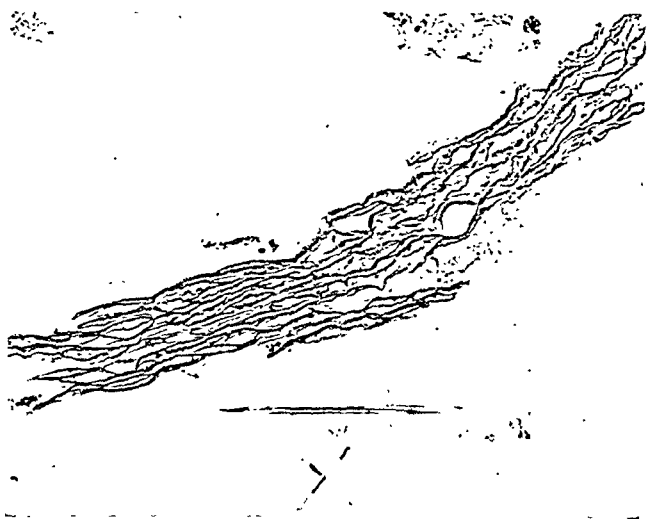


Fig. 8.—X 180. Large plaque of cornified epithelium; the origin of the compressed vaginal spindles is from these plaques.

count in the menstrual blood ranged from 1200 to 5200. In other words one or two things must have happened, either the white blood cells when they escape in the menstrual blood degenerate very rapidly or that the white blood cells do not leave the uterine blood space in the proportion that they are present in the circulating blood. Whether they leave the capillaries and remain in the tissues to perform some reparative function or whether they wander back into the blood stream, cannot at present be answered. It is also possible that because of their greater density they lag behind, adhering closely to the cervical wall and so do not appear in the streaming blood, or that they agglutinate to form small blood clots, the predominating constituent of these clots being the white blood cells.

To account, therefore, for the increase in the number of white blood cells found in the menstrual blood obtained in the vagina over that as it issues from the cervix, some other source of origin than the blood itself must be considered. It would seem most likely to account for this finding in the basis of an exudation through the vaginal mucosa (Fig. 9).

In some instances the number of polynuclear leucocytes was so great as to suggest histologically, pus. In practically all these cases inflammatory factors

TABLE I. SHOWING PERCENTAGE VARIATION IN THE OCCURRENCE OF UTERINE AND VAGINAL ELEMENTS ON SUCCESSIVE MENSTRUAL DAYS

	FIRST DAY	SECOND DAY	THIRD DAY	FOURTH DAY
Uterine epithelium	50%	74%	54%	4%
Uterine stroma	75%	90%	91%	50%
Vaginal spindles	95%	95%	82%	100%
Vaginal plaques	50%	72%	55%	25%

were present, either as pelvic exudates or diseased adnexa or cervixes. On the other hand, in a number of cases, when inflammatory pelvic disease was diagnosed, the white cell content of the vaginal menstrual blood did not contain an excess of leucocytes. Just why there should be this variation at present cannot be determined.

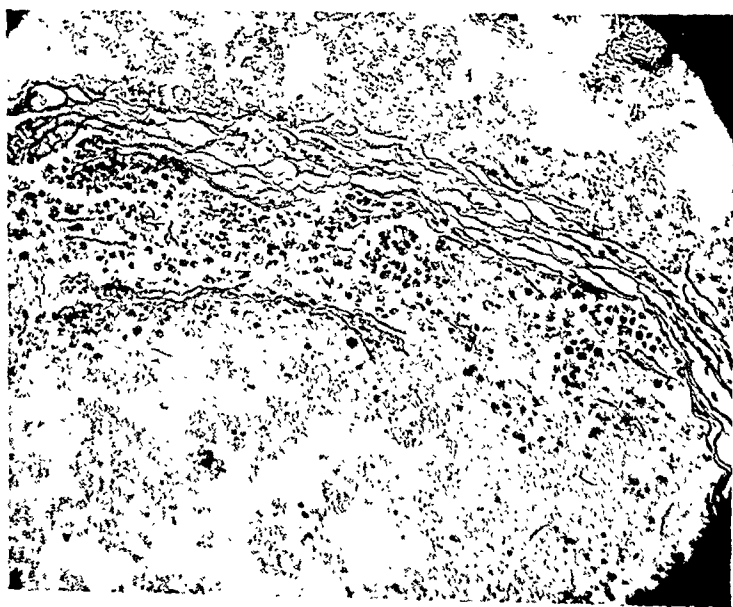


Fig. 9.—X 200. Vaginal plaque, infiltrated with polynuclear leucocytes showing the penetration of the mucous membrane by leucocytes, and the mechanism by which the leucocyte count in the vaginal blood is increased.

We find in the vaginal menstrual blood a definite number of elements which are sufficiently characteristic and stable to enable us to diagnose with certainty a menstrual blood from other types of genital bleeding.

To contrast with the above results we present here the findings of a study of 100 specimens of vaginal blood, presumably nonmenstrual in character.

The blood was obtained and prepared with exactly the same technic as used in the study of the menstrual blood. The same constituents were studied, namely, the uterine epithelium, both the glands and the stroma, the vaginal epithelium, and the leucocytes. It was striking that whereas in the series of bloods obtained from patients who were menstruating, the presence of either uterine stroma or glands were observed as high as 90 per cent on the first three days, in this series of 100 cases they were only found in fourteen instances. Uterine epithelium was found

4 times and stroma 10 times. In the 4 instances where epithelium was found, stroma was also present, so in reality in 10 cases only was glandular tissue and stroma either alone or in combination present.

If we examine the cases showing uterine epithelium in the vaginal blood we find that in one case the history suggested the possibility of an ectopic pregnancy, and an exploratory curettage done one day after the blood was obtained for examination, showed uterine mucosa typically that of a normal menstrual phase. In two other cases the bleeding that caused the patient to consult the physician, occurred approximately one month after a miscarriage and may properly be suspected to be a normal period. The fourth case was the first bleeding after a long period of x-ray amenorrhea, which may also be classed in all probability as a normal period. In those 6 cases in which only a stroma was found, one represented the eighth day of a period of bleeding that had started six weeks after the last regular period. The interpretation of this case must be left open. The second and third cases had a history of bleeding irregularly for two months. The blood obtained for examination might have been a menstrual exacerbation during a metrorrhagia. The fourth case was similar to the above two except here the bleeding was classed as functional and had persisted for a long time. In this instance also we might be justified in interpreting the discharge at the time of examination as a menstrual exacerbation. The other two instances were in cases that had been treated with x-ray to produce an amenorrhea and the blood was obtained at the first period after the amenorrhea. These two specimens could also be classed as probably menstrual bloods.

It will be seen that in those specimens where either stroma alone or in combination with uterine epithelium was found, we were in all probability dealing with menstrual blood. These results coincide very well with the previously mentioned results obtained in a study of normal menstrual blood.

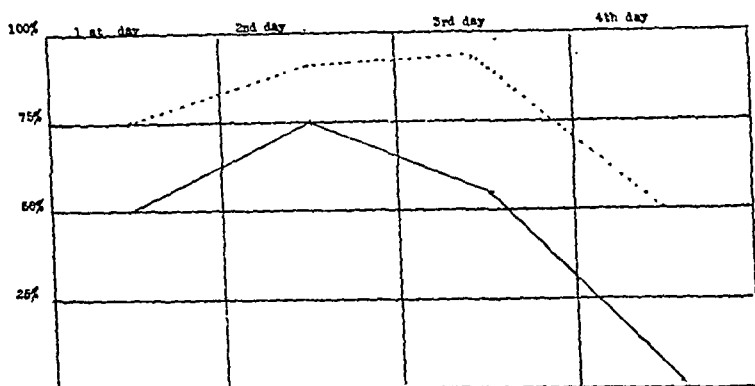
In the remaining 90 cases the specimens were obtained from women with varying types of uterine fundal bleeding. None of the specimens as far as we could determine were menstrual in type. In this group were represented such conditions as incomplete abortions, metrorrhagia from fibroids, metrorrhagia with no demonstrable pelvic lesion, ectopic pregnancy, endometritis, diseased adnexa, etc. In other words, all types of gynecologic cases associated with fundal bleeding. In none of these 90 cases did histologic study of the hemorrhagic discharge show uterine epithelium or stroma.

The finding of the vaginal epithelium either as isolated cells, the so-called spindles or in plaques was not common. In 19 cases plaques were found, mostly of small size and in 29 cases vaginal spindles were present. In every case where uterine epithelium or stroma was present, vaginal epithelium both as spindles and plaques were also found. As we have shown above these cases with uterine elements present were in all probability cases that were menstruating.

We have but 19 cases, as the ones showing uterine epithelium have already been discussed. Of these 19 cases, 9 had vaginal plaques and spindles and 10 vaginal spindles only. In a number of these cases the vaginal spindles were few in number. This finding of a few isolated cells may have no bearing on a vaginal cycle. It is possible that normally in the vagina there is a constant slight desquamation of vaginal epithelium and that in these instances we were fortunate in our examination to find the cells in the specimens studied. Further, it is possible that because of the blood in the vagina a certain amount of maceration and desquamation takes place which we detect as vaginal spindles or even as plaques. Another possible explanation for the occurrence of vaginal spindles and plaques in these bleeding cases may be that the bleeding even though it represented a pathologic process yet took place during the premenstrual time and thus the vaginal epithelium

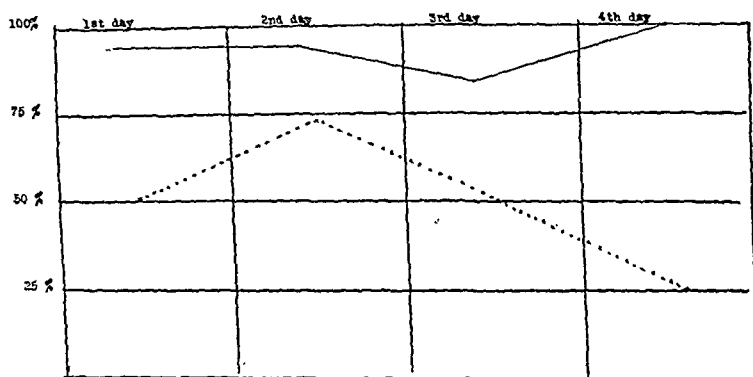
found represented the physiologic desquamation that presumably takes place at that time. On the other hand, it might be possible that some instances of bleeding with vaginal plaques present, represent a menstrual phase during a period of metrorrhagia, the menstrual process resembling that described by Corner as occurring at times in the *Macacus* and not associated with ovulation, uterine mucosal hypertrophy, and desquamation. Finally some of the specimens that contained vaginal epithelium were obtained from patients who had had incomplete abortions and in whom the lochia would naturally contain vaginal epithelium as a part of the reparative postpartum process.

GRAPH A



Graph A.—Graph showing variation in occurrence of *uterine* mucosa in the menstrual blood. Dotted line represents stroma. Solid line represents epithelial elements.

GRAPH B



Graph B.—Graph showing variation in occurrence of *vaginal* mucosa in menstrual blood. Dotted line represents vaginal plaques. Solid line represents vaginal spindles.

The leucocyte count of the vaginal blood in these nonmenstrual cases showed a decided difference from the leucocyte count of the menstrual blood. The nonmenstrual cases showed the normal proportion of leucocytes in the blood as it issued from the cervix, except in a few cases where there was a marked increase in the number of polynuclear leucocytes. In these cases there was a coincident cervical disease. In two cases of diseased adnexa associated with cervical disease, there was a polynucleosis in the blood, as it escaped from the cervix and in the vaginal blood. The *menstrual* vaginal blood as has been pointed out, presents an increased polynuclear count due to transvaginal migration of leucocytes.

In fourteen cases of metrorrhagia not associated with fibroids and with no definite pelvic lesion, curettage was done either immediately after the blood was obtained

or twenty-four hours later while the patient was still bleeding. In none of these cases was uterine elements found in the vaginal blood, and all the curettings showed hyperplasias of the endometrium and cystic dilatation of the glands. There was no evidence of any desquamation, necrobiosis or other histologic sign of a menstruating uterus. Yet these patients were bleeding and bleeding profusely in many cases. We must conclude from this that in the type of case described, a metrorrhagia with no demonstrable pelvic lesion, the mechanism of the bleeding is different from that of the normal menstrual bleeding.

This study would indicate that the hemorrhagic vaginal discharge not due to menstruation, differs so decidedly in morphology from the menstrual blood that the two can be differentiated by histologic examination.

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(For discussion, see page 439.)

## OBLITERATION OF THE VERMIFORM APPENDIX

### A CLINICOPATHOLOGIC STUDY

BY C. ALEXANDER HELLWIG, M.D., WICHITA, KANSAS

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A REVIEW of the surgical literature of the last fifteen years reveals that no study has been made of obliteration of the appendix. This is surprising, because atresia of the appendix is not a rare condition, and there is no unanimity of opinion in regard to its nature.

In his monograph on appendicitis, Royster (1927) comes to the conclusion that obliteration of the appendix may result from a chronic pathologic process or from physiologic atrophy. Aschoff, on the other hand, considers every obliteration of the appendix a sequel of acute appendicitis. The practical importance of the question whether the atresia of the appendix is a physiologic or pathologic condition, is obvious. The removal of an obliterated appendix will cure the patient, if it is due to inflammation; whereas no relief of the symptoms can be expected after appendectomy, if the atresia is a result of physiologic atrophy.

The object of this study was to determine which one of the two different views is better supported by anatomic and clinical facts. The

material examined consisted of 60 obliterated appendices removed at St. Francis Hospital, between November, 1924 and October, 1928. During this period 859 appendectomies were performed.

Immediately after removal at operation the pathologic specimens were preserved in 10 per cent formalin, dehydrated in alcohol and embedded in paraffin. Sections were made from the distal, middle, and proximal thirds of the appendix. After noting gross appearance and microscopic features, the history, clinical and operative findings were abstracted.

*Frequency.*—Our 60 cases of atresia out of 859 appendices obtained at operation give a percentage of 7 per cent. This cannot be compared, of course, with the incidence of atresia as seen in autopsies (25 per cent). V. Redwitz found 6 per cent, Warren 6.5 per cent of the surgical appendices obliterated. The difference between autopsy and operative material is elucidated by the observations of Miloslavich and Namba who saw this condition in 30 per cent of the autopsy cases, but only in 7.5 per cent of the appendectomies.

All authors who studied the subject on autopsy material agree that the incidence increases with advancing age. This influence of age led Ribbert, Zuckerkandl, and Sudsucki to the conclusion that the atresia is a physiologic age involution. We agree with Senn that we must expect more cases of obliterations in old people, if we regard them as a sequel of inflammation because the longer the person lives, the greater the liability to suffer from acute appendicitis. Faber points out that the atresia of the appendix is like other scar formations which remain throughout life, once they are formed. Gruenfeld, for instance, found perigastric scars, following stomach ulcer, in 32 per cent of women older than sixty years, but nobody would conclude from these findings that stomach ulcer is more common in old age.

The following table shows the number of obliterated appendices as found in our series in the different decades of life:

AGE	NUMBER OF OBLITERATED APPENDICES
1 - 10	2
11 - 20	9
21 - 30	24
31 - 40	20
41 - 50	2
51 - 60	3

Most of our patients with obliterated appendices (93.5 per cent) were younger than forty years. The average age of the 60 cases was 29.5 years, the youngest patient was four years old. This is surely not in favor of the view that obliteration of the appendix is due to age involution.

*Gross Appearance.*—Ribbert, Hanseemann and Oppenheim point out that the obliteration, as a rule, is located in the tip of the appendix,



but that the acute appendicitis affects mostly the whole organ, and that therefore the atresia cannot be caused by inflammation. Also in our material the majority of obliterations (56 per cent) were limited to the distal third, but by examination of several hundred acutely inflamed appendices we observed that the acute appendicitis also starts, as a rule, in the distal portion and that in cases where the whole organ is affected, the most extensive destruction is found, almost without exception, in the tip. This explains why the distal third of the appendix is more liable to atresia than the proximal portions where often epithelial tissue remains viable after subsidence of the inflammatory process.

*Microscopic Findings.*—The main argument by which Zuckerkandl, Sudsucki, Oppenheim and others support their view that physiologic involution is the cause of atresia, is the uniform microscopic picture and the absence of inflammatory changes in the obliterated appendices obtained at autopsy. Our own microscopic findings did not harmonize with their descriptions and were far from being uniform.

*Mucosa.*—In 22 per cent of our specimens which appeared solid to the unaided eye the microscopic examination revealed a narrow chink without epithelial lining (Fig. 1). In six cases this small lumen appeared empty, in two it was filled with leucocytes and round cells, in two others, fibroblasts with collagen fibers were growing from the wall into the lumen (Fig. 2).

In the other 47 cases no trace of a lumen was detected by microscopic examination. But one-third did not present the uniform picture as described by Ribbert either. In 9 the center consisted of cellular granulation tissue and in 6 cases it was infiltrated by numerous eosinophile leucocytes.

*Lymphoid Tissue.*—The amount of lymphoid tissue varied widely in our material. Forty-one specimens had well preserved lymphoid tissue in the center, six of them real lymph follicles with germinal center, which disproved Oppenheim's theory that the atrophy of the lymph follicles is the primary cause of the atretic process. The decisive factor for the varying amounts of lymphocytes in the solid center is the extension of the ulcerative process which led to the atresia of the appendix. The longer the obliteration persists, the more the lymphoid tissue will disappear, but we do not agree with Oberndorfer, that hyperplastic lymph follicles and lymph vessels filled with round cells are evidence of chronic inflammation. Both can be present as well in the normal appendix.

*Submucosa.*—The two layers of the submucosa are easily recognized, even in the obliterated appendix, as long as the lymphoid tissue of the inner layer is preserved. In this case the dense fibrous external layer with islands of fat tissue is very distinct. Sudsucki attempted to differentiate three forms of atresia, according to the varying amounts of fat tissue in the submucosa. Our findings do not confirm this view.

A scarcity of lymphocytes near the blood vessels in the external layer of the submucosa must not be regarded as sign of inflammation, as they are frequently found also in normal organs. A definite increase of cells was present in 25 of our specimens. We noted very many lymphocytes in 8, many lymphocytes in 9 and very cellular granulation tissue with fibroblasts, round cells and capillaries in 8 obliterated appendices.

*Internal Muscle Layer.*—In the normal appendix the inner muscle ring is not

sharply defined from the mucosa, little muscle bundles being separated by fibrous tissue. The spaces between the muscle tissue are normally very thin and harbor

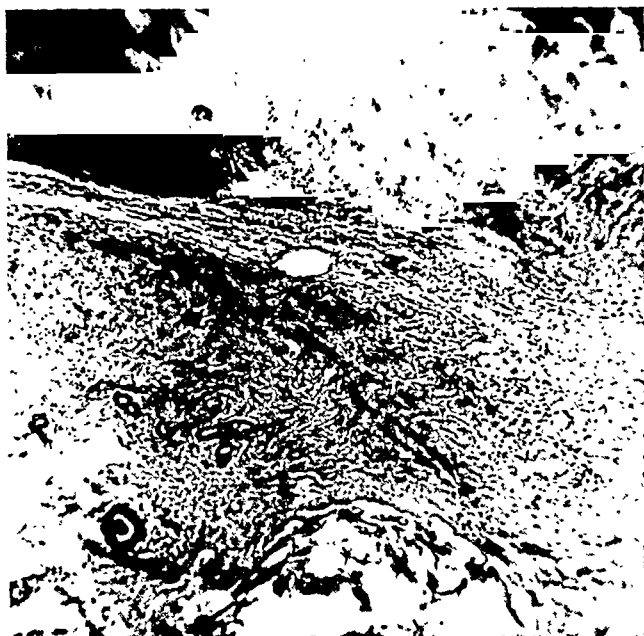


Fig. 1.—Center of obliterated appendix. Scar tissue is replacing the former lumen and the mucosa. A very fine lumen is recognized by microscopic examination.



Fig. 2.—Distal third of appendix, four weeks after first attack of appendicitis. The mucosa is completely destroyed and fibroblasts with collagen fibers are filling in the lumen.

only occasionally eosinophile leucocytes and round cells. In 41 of our 60 obliterated appendices the inner muscle bundles were split in a marked degree which was

evidenced by comparing slides from the obliterated and patent portion of the same specimen. In 13 appendices the muscle bundles were separated by young granulation tissue with extensive cellular infiltration, in 19 by thick fibrous spaces and in 6 cases large scars interrupted the whole muscle ring and were regarded as residues of the intramural abscesses, according to the idea of Mundt and Aschoff.

*External Muscle Layer.*—In the normal appendix the longitudinal muscle layer often looks eccentric in the cross-section, one part of the circumference being thicker than the other. Near the insertion of the mesoappendix the muscle bundles are sometimes separated by fibrous spaces. Pathologic enlargement of the inter-muscular spaces differs from the normal in that it involves mostly the whole circumference. This "segmentation" is regarded by Aschoff as a very reliable and sometimes the only remaining sign of a healed appendicitis (Fig. 3). It was present in 32 of our 60 cases. More recent inflammatory changes of this layer were



Fig. 3.—Thick fibrous spaces in the external muscle layer of an obliterated appendix. This "segmentation" together with thickening of the serosa by scar formation is often the only persistent sign of a healed appendicitis.

seen in 13 specimens, in two appendices follicle-like groups of round cells had formed between the muscle bundles.

*Serous Layer.*—The serosa of the normal appendix is a very thin layer of loose connective tissue, covered with the peritoneal endothelium. Often fat tissue is noticed in the serosa, opposite the insertion of the mesoappendix. Following a phlegmonous appendicitis the thickening of the serosa by scar tissue recedes slowly, but may remain as a persistent sign of a healed inflammation. In 45 of the 60 obliterated specimens the serosa was much thicker than normal and only 8 were without cellular infiltration. In 37 the cellular infiltration was abundant and consisted of neutrophile and eosinophile leucocytes (16 cases) or small round cells (21 cases). The latter were grouped, as a rule, around blood vessels and formed in 5 specimens larger groups resembling lymph follicles. We agree with Nishikawa that a new formation of lymphoid tissue in the external layers of the appendix is a valuable sign of healed inflammation.

*The Nonoccluded Portion.*—In the 33 specimens with partial atresia the sections of the patent portions furnished most interesting data. More than two-thirds

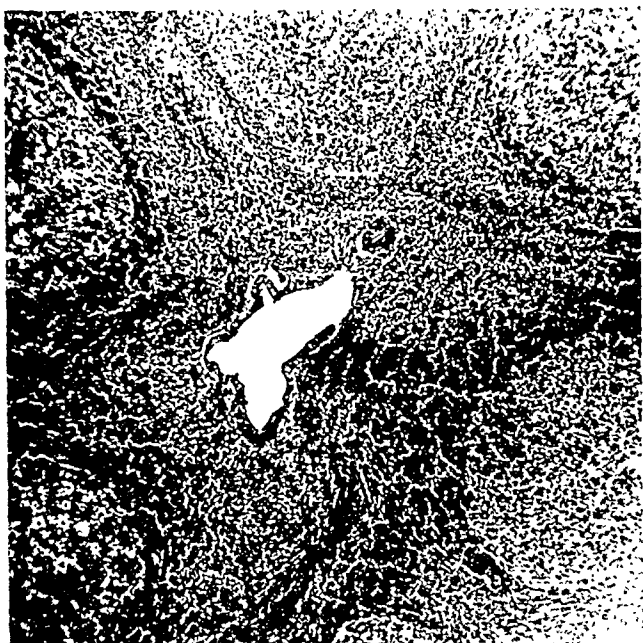


Fig. 4.—Stenosis of the lumen and incomplete repair of the epithelium in the proximal portion of a partially obliterated appendix. The hyperplasia of the lymph follicles is no sign of inflammation.



Fig. 5.—Patent portion of a partially obliterated appendix. The epithelium and lymphoid tissue is completely destroyed and replaced by granulation tissue. Acute attack five weeks previous to the operation.

showed pathologic changes. Twelve had a marked stenosis and distortion of the lumen, with low epithelium and few or no glands (Fig. 4). In 8 other appendices

the epithelial tissue was completely missing and cellular granulation tissue surrounded the lumen (Fig. 5): If the process would go unchecked in these cases, obliteration of the entire lumen would be the terminal stage. In three specimens we found a typical primary focus in the mucosa of the patent portion (Fig. 6). A condition which Aschoff described recently as rudimentary appendicitis was observed in 4 appendices, where leucocytes infiltrated the wall, especially the muscle layers, but the portal of entrance could not be detected.



Fig. 6.—Primary focus in one recessus of the patent portion. The last of several attacks occurred three days before the operation.

#### CLINICAL DATA

In our cases the following clinical diagnoses were made:

Appendicitis	
acute	12
subacute	7
chronic	8
recurrent	19

Total	46
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#### Other Abdominal Diseases

Duodenal ulcer	1
Cholecystitis	2
Salpingitis	7
Retroflexion	3
Prolapse of uterus	1

Total	14
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In the second group six cases are included in which a diagnosis of appendicitis, complicated by some other intraabdominal disease was made. Forty-eight of all our patients with obliterated appendices had definite acute attacks of pain, months or years prior to the operation, which were interpreted as acute appendicitis. In the history of the other 12 cases severe attacks were not mentioned, but only slight recurrent discomfort, indigestion, backache, painful menstruation were

complained of, or the patients were entirely unaware of a serious abdominal disorder.

*Acute Appendicitis.*—Eight of the 12 patients with clinical diagnosis of acute appendicitis complained of several definite attacks previous to the operation. If we consider leucocytic infiltration of the wall as evidence of acute appendicitis, then the pathologic findings did not harmonize with the clinical diagnosis in one-half of these 12 cases. In two specimens the leucocytes were numerous only in the external layers of the completely obliterated appendix, and we are inclined to believe that this periappendicitis was secondary to some other intraabdominal inflammation, in spite of the fact that the operation did not reveal it. Five appendices which belong to this group were completely obliterated and did not show any leucocytic infiltration. It raises the question whether the symptoms which led to the clinical diagnosis of acute appendicitis were due to some other pathology of the appendix or whether they were caused by pathology of some other organ. At least in one of these cases which had a leucocyte count of 18,000, the completely occluded appendix could not account for the severe attack. V. Redwitz found in all obliterated appendices of his series endarteritis of the appendiceal blood vessels and expresses the belief that a spasm of the diseased vessels could produce severe attacks of pain. Since only one of 5 cases with clinical diagnosis, but without pathologic evidence of acute appendicitis, presented these endarteritic changes, we do not feel justified in accepting his explanation. Also Rohdenburg's view that the painful attacks are due to compression of ganglion cells by scarring in the obliterated appendix seems questionable, because no other part of the body is known where fibrosis produces acute attacks of pain.

The problem of visceral sensibility is far from being solved. The opinions are still divided whether the sympathetic fibers of the intestinal wall are able to transmit painful stimuli or whether only the cerebrospinal nerves of the lateral peritoneum are responsible for abdominal pain. We agree with Goldscheider, Mueller, and others that the visceral pain can originate in the intestine itself. The work of H. Braun and Schade seems to demonstrate that it is not so much the mechanical, but the physicochemical irritation of the sympathetic nerves by the inflammatory exudate which causes the pain in inflammation. This of course will not be the case in completely occluded appendices, except where acute inflammation spreads from some other intraabdominal organ to the external layers of the wall, as is often seen in salpingitis. We shall understand further that the healing stage of acute appendicitis can also be accompanied by pain, if we keep in mind that healing wounds of the skin are often hypersensitive to the slightest touch. The passage of fecal material or muscular contraction of the organ accounts in all probability for the discomfort in the recovering stage of appendicitis.

*Subacute Appendicitis.*—This was diagnosed by the clinician in 7 cases. In two of these, cramp-like pains were present for several years, often at times of menstruation. Two patients complained of mild attacks of pain, two and three weeks respectively before the operation, and did not remember any former attacks which could account for the complete atresia of their appendices. In this group was also a four-year-old boy who took sick suddenly five weeks prior to the operation. The whole mucosa of the appendix was destroyed and replaced by cellular granulation tissue. Four other cases showed microscopic evidence of a recent inflammation.

*Recurrent Appendicitis.*—Senn who introduced the term "Appendicitis obliterans" pointed out that the most constant symptoms which attend this form are recurrent acute exacerbations of short duration and persistence of soreness and tenderness in the region of the appendix during intermissions. All but two of our 19 patients in this group had such a history of repeated typical attacks of severe character. Six patients had total atresia of the appendix and in more than  $\frac{2}{3}$  only the distal third was occluded. The appendix of one patient who had the last of several attacks

two days before the operation showed in the patent portion a typical primary focus in the mucosa and some leucocytic infiltration of the wall. In three other partially obliterated specimens part of the mucosa was replaced by cellular granulation tissue and many eosinophile leucocytes were present in the wall. Leucocytic infiltration was not found in two specimens in spite of the fact that the last attacks occurred one and two weeks respectively previous to the appendectomy.

*Chronic Appendicitis.*—An exhaustive inquiry into the nature of chronic appendicitis is not within the scope of this paper. After reviewing over 100 microscopic sections of so-called chronic appendicitis, I agree with Aschoff that morphologic evidence of chronic appendicitis proper does not exist. In the cases where the appendix is diseased either repeated mild acute inflammations or the healing stage of acute appendicitis are the pathologic bases of so-called chronic appendicitis. On the other hand, I believe that the tendency of modern writers to abolish entirely the clinical diagnosis "chronic appendicitis" is too radical. It must be kept in mind that even purulent appendicitis can occur without severe clinical symptoms and the convalescent stage of an acute attack can last several months. With such a conception a lingering course of appendicitis without acute symptoms is readily conceivable, and for these cases the term "chronic" seems as much justified as in chronic tonsillitis, salpingitis, or osteomyelitis. We must admit, however, that very often the clinical diagnosis of chronic appendicitis cannot be confirmed by any pathologic findings in the appendix. In my study of over 100 cases, diagnosed clinically as chronic appendicitis, only 51 per cent of the specimens showed inflammatory changes and in a large clinical material Mehlhor found only 40 per cent of his patients relieved by appendectomy.

Of our occluded appendices there were 8 obtained from patients with so-called chronic appendicitis. Five in this class had several acute attacks and their histories did not differ in any sense from those with recurrent appendicitis. In two the painful attacks occurred at the time of menstruation, one patient complained of stomach trouble which had no relation to meals. Three appendices were completely occluded, five only in the distal third. In two specimens no recent inflammatory changes were found, one showed only marked endarteritis in the subserosa and submucosa. A typical primary focus with leucocytic infiltration in the patent portion was revealed in one case in which the last of several attacks occurred three days previous to the operation. In one other case the presence of cellular granulation tissue with many eosinophile leucocytes in the wall conformed to the history of his last attack one week before the operation. Two appendices in this group showed extensive perivascular infiltration of lymphocytes in the serosa.

*Other Abdominal Diseases.*—In the case complicated by duodenal ulcer the obliterated appendix had granulation tissue in the mucosa and submucosa and many eosinophile leucocytes were infiltrating the whole wall. Four appendices were obtained in the course of operation for cholecystitis. In one of these, cellular granulation tissue replaced one-half of the mucosa in the patent portion and the other layers of the wall were infiltrated by numerous leucocytes. One appendix showed extensive infiltration of the subserosa by eosinophile leucocytes in addition to large groups of small round cells.

The difficulty of differentiating clinically between acute appendicitis and salpingitis is well known, as inflammation of one of the two organs can spread to the other. Coexistence of a healed appendicitis and of salpingitis is no argument for considering salpingitis as a sequel to appendicitis. In primary appendicitis it may be expected that only the external layers of the tube are involved and that the mucosa is without inflammatory changes. On the other hand, gonorrheal salpingitis will cause as a rule only infiltration of the subserosa of the appendix without affecting the inner layers. In three of our seven cases which were diagnosed as salpingitis, the microscopic examination suggested only a secondary involvement of the tube following appendicitis.

Four of our obliterated appendices were obtained at operations for retroflexion and prolapse. One of the patients complained of pulling sensations, another of stomach trouble, the third of pain in both sides and the fourth felt discomfort only when standing. Except for round-cell infiltration of the subserosa in one specimen, no inflammatory changes were found in this group. It raises the question whether the discomfort of these patients was due to the misplaced uterus or to recurrent mild attacks of appendicitis which resulted in atresia of the appendix.

#### SUMMARY

Of 859 appendices obtained at operation 60 or 7 per cent showed atresia of the lumen. In 56 per cent only the distal third was occluded, in the others the whole organ.

The microscopic picture of the obliterated appendices did not correspond to the descriptions as given by Ribbert, Sudsucki and Oppenheim who studied autopsy material. Far from being uniform, it was of the greatest variety. In more than one-half of the cases leucocytic infiltration and cellular granulation tissue was found which indicated that an inflammatory process had not completely subsided or that a healing stage of acute appendicitis was complicated by recurrence. Signs of a healed appendicitis were found in about  $\frac{2}{3}$  of the specimens and consisted of scar formation in the external layers. The histologic examination of the nonoccluded portion revealed pathologic changes in  $\frac{2}{3}$  of the partially obliterated appendices and in one-half of these the inflammatory changes were recent.

No morphologic evidence of chronic appendicitis proper was found in our material, but all stages of transition from acute purulent inflammation to the healing stage and to terminal fibrosis were present, leading to the conclusion that the atresia is the final stage of ulcerative appendicitis in which the epithelial tissue is completely destroyed.

The average age of our patients was twenty-nine and five-tenths years, the youngest being four years old. Forty-eight patients (79 per cent) complained of recurrent acute attacks which were interpreted as attacks of appendicitis. In 12 the clinical history was not typical. The clinician's diagnosis was in 46 cases, appendicitis alone; in 6, appendicitis complicated by some other intraabdominal disease; in 8 patients a lesion of the appendix was not expected.

#### CONCLUSIONS

The clinical as well as the morphologic data in our series are in harmony with the view held by Aschoff that atresia of the appendix is due to acute appendicitis.

An appendix with complete obliteration will not undergo inflammation again and its removal will not relieve the patient of his symptoms. An appendix with partial obliteration, on the contrary, is disposed to recurrent inflammation, because the stenosis of the nonoccluded portion and the fibrosis of the muscle layers favor retention of its contents and bacterial invasion of the mucosa.



## CASE OF GRAVID UTERUS DIDELPHYS RESULTING IN STREPTOCOCCIC PERITONITIS\*

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THE medical literature is replete with articles on this subject, and almost every textbook on obstetrics describes the various forms of the double uterus, as the uterus septus, bicornis, didelphys, etc., yet very little is written about the pathologic conditions resulting during



Fig. 1.—Normal attitude of fetus in a normal uterus.

pregnancy in such women. The following case report is therefore of interest:

Mrs. M. K., aged twenty-five, primipara. In her fifth month of pregnancy, was examined in the prenatal clinic, and found to have a double uterus. The vagina was divided in two parts by a septum, and in each part a cervix was seen. By palpation a uterus bicornis was mapped out, the right uterus being impregnated. Her pelvic measurements as well as her general condition were normal.

\*Read before the North Bronx Medical Society.

On March 9, 1928, then six and one-half months pregnant, she suddenly developed severe pain in the right lower abdominal region, with chills and vomiting. Her temperature was 104° F. The pain becoming progressively worse, she was taken to the hospital.

Physical examination revealed an acutely ill female adult, with marked tenderness over the right lower abdomen. The right cervix was open, admitting one finger and bleeding, with membranes intact. The left cervix was closed. The fetal heart rate was 180 per minute.

Previous history negative. Menstruation began at the age of fourteen, regular thirty day type, lasting four to six days; she always suffered with premenstrual



Fig. 2.—Deviation of fetus to right in uterus didelphys.

pain. Her last period was Aug. 29, 1927; patient now six and one-half months pregnant, para i, no miscarriages. Abdominal examination showed the fundus uteri enlarged, palpable above the umbilicus. Rigidity, pain, and rebound tenderness were localized over the right lower quadrant. There were no intermittent uterine contractions, probably because the patient had received morphine before admission to the hospital. A blood count showed Hb. 70 per cent; leucocytes, 24,000; neutrophils, 93 per cent; and lymphocytes, 7 per cent.

Provisional diagnosis of acute appendicitis was made; and exploratory laparotomy decided upon.

On opening the abdomen, a thin, yellowish, odorless fluid was noticed. The appendix was normal, but the right ovary was found very much enlarged, inflamed, and appeared necrotic. A rubber tube drain was inserted, and abdomen closed.

The blood culture as well as the culture of the abdominal fluid showed *Streptococcus hemolyticus* in eighteen hours; colonies per c.c. of blood too numerous to count.

Postoperative diagnosis: General peritonitis with *Streptococcus* (hemolyticus) bacteremia.

On March 10, at 5:00 A.M., a premature stillborn male child was delivered spontaneously. The placenta though delivered from uterus spontaneously, had to be removed from vagina manually. The patient died March 13, 1928.

#### AUTOPSY FINDINGS

##### (Positive Findings Only)

The abdomen was distended with greyish cloudy liquid. The uterus was enlarged and divided by a septum into two unequal parts. The right 15 by 7 by 5 cm.,



Fig. 3.—Left tube showing normal villi and normal wall.

with the cervix 3 cm. in diameter; the left 11 by 5 by 5 cm., with the cervix 2 cm. in diameter. The peritoneal surface was smooth, the wall thick and soft, 1.4 cm. thick; the septum was 1.2 cm. thick, soft and in places necrotic. The lumina were filled with necrotic material.

The right ovary measured 5 by 4 by 2 cm., greyish, soft, necrotic and covered by fibrinopurulent exudate. The right tube and fimbria were thicker than the left. The left ovary measured 3 by 3 by 1.5 cm., and the tube appeared normal. The broad ligaments appeared normal on both sides.

Histologic examination showed in the right ovary coagulation necrosis with a demarcating zone of polymorphonuclear leucocytes with fibroblasts, and endothelial cells. The rest of the ovary contained hemorrhage and congested vessels. The left ovary showed neutrophilic infiltration near the surface and slight congestion of the vessels. The right tube presented in the subserosa perivascular infiltration of endothelial leucocytes, lymphocytes, and few neutrophils, with capillary congestion. The muscularis was similarly affected, and in addition showed edema. The

mucosa showed the villi thickened by infiltration of endothelial leucocytes, lymphocytes, and neutrophils. In the left tube there was infiltration of polymorphonuclear leucocytes in the perivascular spaces and in the tips of the villi. In the uterus the endometrium showed coagulation necrosis, and polymorphonuclear leucocytes. Many of the vessels were thrombosed, and there were areas of hemorrhage. The muscle coats in the myometrium were separated by edematous fibrous tissue, with perivascular infiltration of endothelial leucocytes, lymphocytes and neutrophils. The muscle fibers were degenerated. The septum was more affected than the rest of the myometrium. The condition of the endometrium was the same in both uterine cavities each containing sloughing decidua.

**Analysis of the Pathologic Findings:** The right ovary shows gangrenous oophoritis of some duration, produced possibly by disturbed circulation, together with infection, as evidenced by the size of the organ, the engorged vessels, and hemorrhage, suggesting torsion or massive embolism.

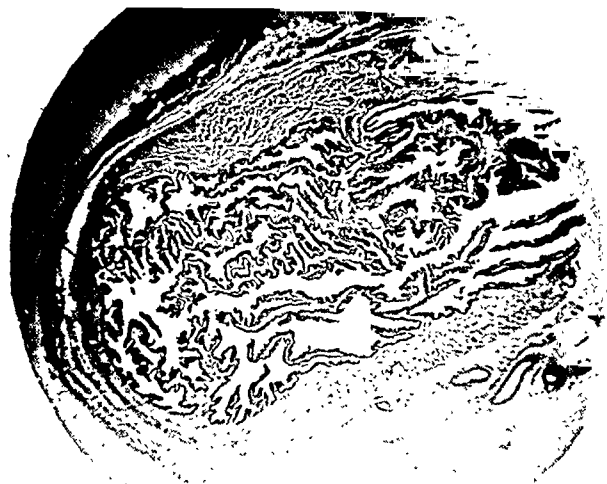


Fig. 4.—Enlarged right tube showing villi thickened by purulent infiltration.

The diffuse peritonitis very likely originated in the right ovary, since the uterine serosa was free from exudate. On the other hand, the histologic picture of the uterus is that of a septic endometritis, with perivascular infiltration of endothelial leucocytes in the myometrium, indicating an inflammation of longer duration. This indicates a possibility also, that the peritoneum was infected through the ostium of the right tube.

The immediate fatal issue was very likely the result of *Streptococcus hemolyticus* bacteremia.

#### DISCUSSION

The prerequisites of a normal generative process are healthy, normally developed genitalia. Developmental anomalies of the female genitalia are often obstacles to conception, and when conception does occur, the development of the fetus is frequently interfered with.

Finally, when the pregnancy comes to term such anomalies may become causes of serious dystocia, endangering not only the life of the child, but also that of the mother.\*

The developmental anomaly of a double uterus, due to the failure of fusion of the müllerian ducts, is often encountered. The uterus didelphys, bicornis, bilocularis, septus, etc., all depending upon the degree of fusion of the müllerian ducts. This leaves the organs of generation in an imperfect state, constituting a most vital problem for the obstetrician.

The appendages of a double uterus are most always in a state of chronic inflammation, and during pregnancy, it constitutes a most inviting place for bacterial invasion. The abnormal position of the child in such a uterus, as we can see from the x-ray (Fig. 2), is often a cause of fetal asphyxia, even before labor sets in; and the deviation of the upper pole of the fetus to one side prevents the lower pole from engaging during labor in a normal position.

Pregnancy in such uteri occurs; even twin pregnancies, one fetus in each cavity of the uterus, were observed. Sometimes such cases go through pregnancy and birth uneventfully. This is the exception; as a rule the birth is interfered with. A retained placenta with severe post-partum hemorrhage is a common occurrence in such uteri. This is due to the lack of decussating muscular fibers from one half of the uterus to the other, the side forming the median line being weaker in structure. The contractile power of such a uterus is not sufficient to expel the placenta, or to obliterate the bleeding sinuses and blood vessels.

Septic emboli are also seen in such uteri. This may be explained by the two uterine arteries not anastomosing as they do in front of and behind a single cervix, behaving similarly to a terminal circulation. Prof. Strassman of Berlin considers these uteri when they become pregnant with the same apprehension as ectopic pregnancy. He advocates an operative procedure before permitting pregnancy, uniting the two halves and forming one uterine cavity; and when pregnancy is discovered early, he empties the uterus artificially, and then performs this plastic operation. In cases of uterus septus, all that is necessary is to cut through the septum.

In our case the necrotic right ovary may have been caused by a septic thrombus in the right uterine artery cutting off the blood supply of the ovary, the blood supply of the latter being mainly by the ramus ovaricus, a branch of the uterine artery.

It also gives us a clear view of the condition of the appendages of the uterus as seen from the microscopic slides. The right pregnant side presents an inflamed condition, whereas the nonpregnant side appears to be normal.

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\*Falls, F. H.: *Am. J. Obst. & Gynec.* 15: 399, 1928.

A mucous plug is still noticeable in the left cervical canal. The general septic condition may have started within the right uterine cavity, entering the blood stream through the veins and lymphatics.

#### CONCLUSIONS

1. Treat pregnancy in a double uterus as a nonruptured ectopic; empty the uterus and correct the maldeveloped organ.
2. If the condition was not discovered until the end of pregnancy a course of watchful waiting must be assumed. Sometimes an uneventful delivery will take place.
3. Be prepared for a severe postpartum hemorrhage, and be ready for a stormy puerperium.

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### THE CLINICAL USE OF VAGINAL SPREADS

BY MAX D. MAYER, M.D., NEW YORK CITY

(*From the Gynecological Service of Mount Sinai Hospital*)

**A**N EXTREMELY interesting and careful study of the vaginal flora, made under the direction of Schroeder, has thrown light upon the biology of the vagina. The study included a combined bacteriologic, chemical, and microscopic investigation.

The following brief report represents an attempt to apply the examination of vaginal smears as a routine procedure, and to determine its diagnostic value in gynecologic cases.

Schroeder, R. Heinrichs, and R. Kessler have gone far beyond the early investigations of Doederlein, Menge, von Jaschke, and others. They have demonstrated the concomitant variation between the hydrogen-ion determination of vaginal secretions and the degree of bacteriologic cleanliness, as well as the morphology of the smears. They have shown that the recognition of the Doederlein bacillus by smear is substantiated by careful plating. From this it appears, therefore, that in a practical method of utilizing the knowledge of a particular vaginal flora in a series of cases, it is unnecessary to use cultural methods or titration.

My study is based upon 600 cases, in each of which smears were taken from within the introitus, the midvagina, the anterior fornix, and the cervix. In each instance a careful history and an examination were included as part of the procedure. Cases in which the diagnosis could not be substantiated by operation or otherwise were not included. The smears were stained by the Gram method. Schroeder in his own routine cases now uses methylene blue. I have not found this sufficient. The smears were examined and described without knowledge, at the time, of clinical data. The patients in the reported series were on the

gynecologic ward in Mount Sinai Hospital; a large number were similarly studied in the Out-Patient Department and in private practice. The series was divided into two groups: (1) a preliminary study of (a) the variations in findings in varying portions of the vaginal tract; (b) the consistency of the findings in the same patient; (c) the proper classification of smears for diagnostic purposes, etc., and (2) the series reported below.

The preliminary study of 300 cases seemed to warrant the division into the following types:

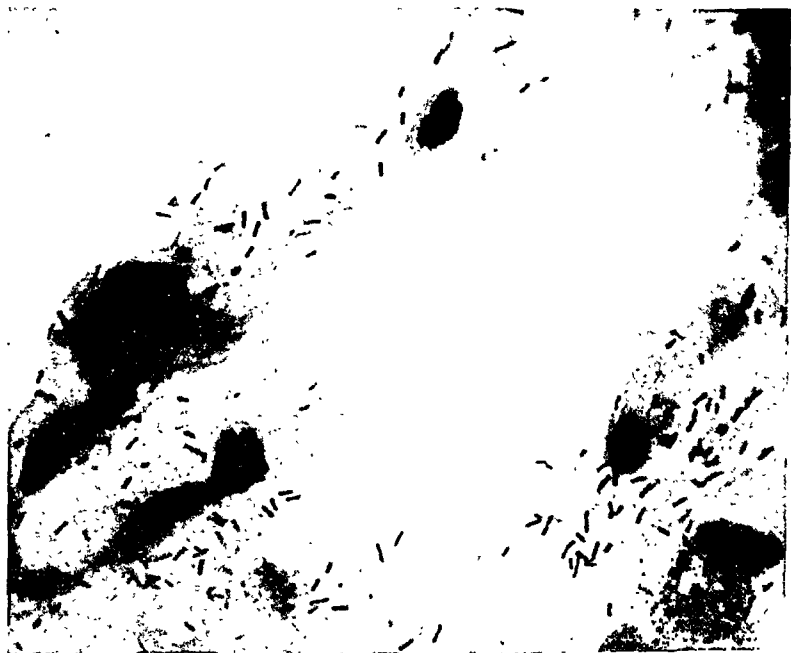


Fig. 1.—Intact virgin Flora 1 moderate number of Doederlein bacilli, some desquamated epithelial cells. This slide is characteristic of a clean, nongravid vagina.

1. *Flora 1*.—Doederlein bacilli only, epithelial cells, with or without some pus.
2. *Flora 2a*.—Doederlein bacilli as well as other bacteria without frank pus.
3. *Flora 2b*.—Doederlein bacilli, other bacteria, with pus.
4. *Flora 3a*.—No Doederlein bacilli present. Bacteria of a single type, or a variegated flora, *no pus*.
5. *Flora 3b*.—No Doederlein bacilli present. Bacteria of a single type or a variegated flora, *with pus*.
6. No bacteria present, débris only.

Flora 1 connotes discharge that is white, but a white discharge does not always signify Flora 1. The correlation between the findings in various portions of the vagina was high. Repeated examinations of any individual showed a high degree of consistency. Coitus even if it had occurred recently seemed to play no appreciable rôle. If other bacteria than Doederlein bacilli were found in any portion of the tract, the smear was not classified as Flora 1; and if Doederlein bacilli were seen in any portion, the smear was classified as Flora 2. The cervical

smears were of importance in the diagnosis of gonorrhea as well as in the evaluation of the upper vaginal smears.

A series of 300 cases was then studied, utilizing the method as a diagnostic aid. Of these, 80 cases had to be excluded because of diagnostic doubt or unsatisfactory smears. An analysis of the remaining cases follows:

Flora 1 was found most often in virgins, in pregnant women, and in uncomplicated menopause cases. In pregnant women, the slides very frequently showed a characteristic luxuriant growth of large, plump Doederlein bacilli, together with large desquamated epithelial cells, nucleated and nonnucleated. The more children a woman had previously borne, the more certainly the presence of Flora 1 signified

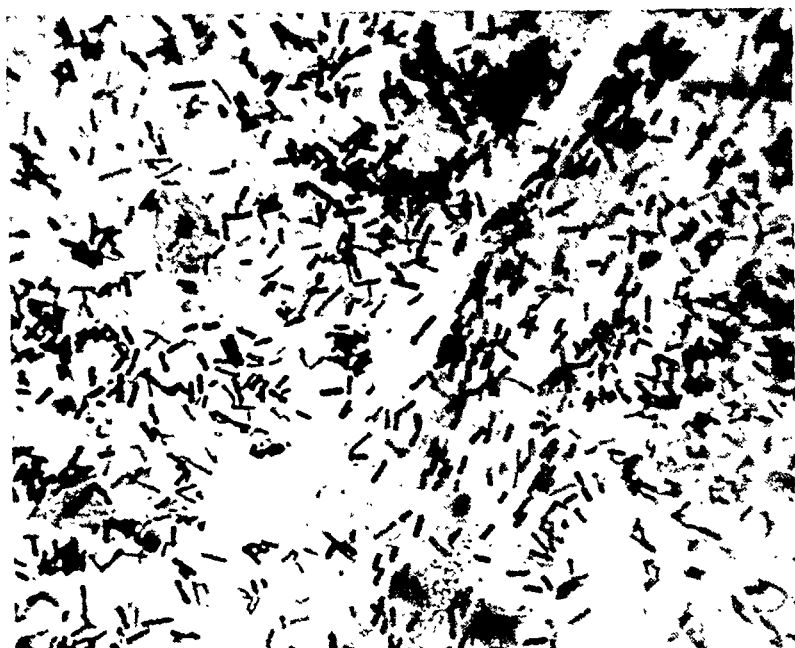


Fig. 2.—Flora 1 luxuriant growth of Doederlein bacilli, desquamated cells. Smear from a pregnancy in a multipara.

gravidity. With repeated pregnancies one may expect to find a more and more contaminated vagina. It is obvious, then, that Flora 1 will have a greater diagnostic value the larger the number of previous births. In intact virgins Flora 1 was invariable.

Flora 2 and 3a without pus were most frequently found in noninfected non-gravid women, most of whom came to the ward for plastic operations or fibromyomas; the characteristic finding in cystoectomies may be due to exposure and contamination through a lax introitus. Cervical carcinoma showed either Flora 3b together with a varying number of monocytes, or debris without bacteria. The number of women with ectopic pregnancies examined, was insufficient to warrant the drawing of conclusions. Bleeding usually interfered with the examination even when a special technic was employed, involving the use of acetic acid. The results therefore disappointed any of the hope entertained of an additional aid in this so frequently troublesome diagnosis.



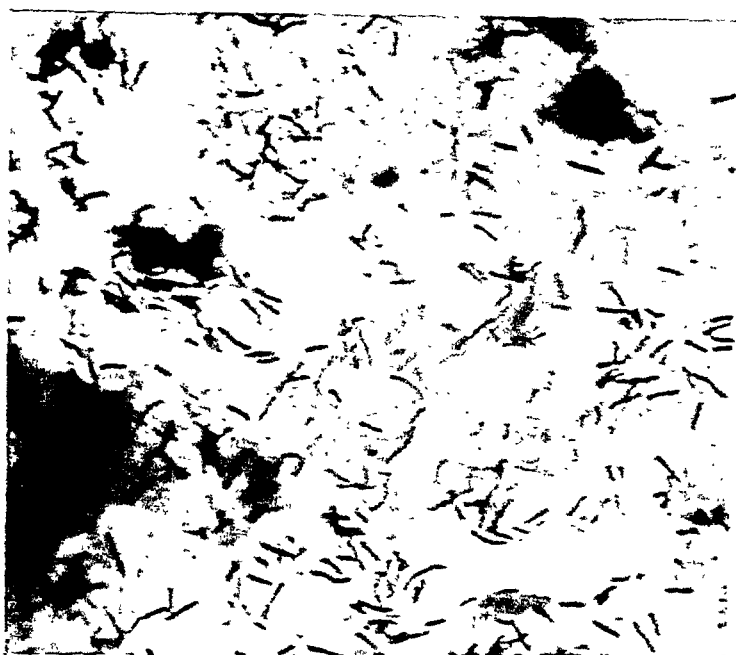


Fig. 3.—Flora in epithelium, practically no pus, some leucocytes, a moderate number of Döderlein bacilli, a few other bacteria; a relatively clean vagina.

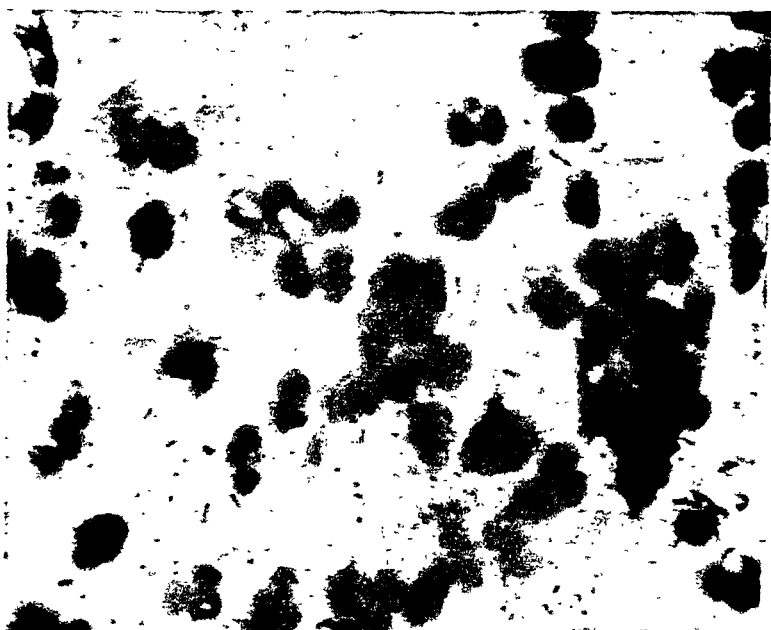


Fig. 4.—Flora in many pus cells, a few Döderlein bacilli, many other bacilli. This woman came into the hospital for cystourethritis. She had had three children, three miscarriages; had been married fourteen years and was separated for three years. It represents an intermediate slide between Flora 3a and Flora 3b.

Of the 220 cases, 201 were compatible with the preliminary impressions. In 19 cases the results were potentially misleading although there was no actual difficulty in establishing a clinical diagnosis in any of these cases. In 19 other cases the smear proved a distinct diagnostic aid. The diagnostic value was greatest in the following instances:

Gravidity vs. fibroid or cyst  
 Gravidity in very obese patients  
 Salpingitis vs. appendicitis  
 Diseased adnexa vs. neoplasm  
 Intact virgin?  
 Clean vs. infected abortion

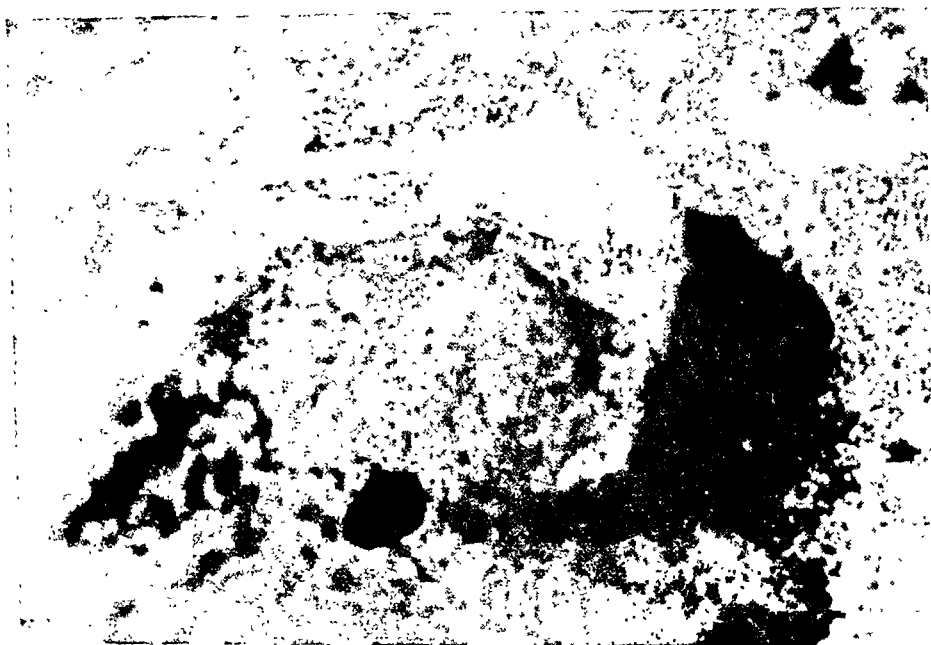


Fig. 5.—Flora 3a innumerable bacteria, gram-positive and gram-negative; no pus. This type of smear was frequently found in noninfected cases.

No case of gravidity was encountered in which Doederlein bacilli were not found, even including 3 cases of gonorrhea complicating pregnancy. (Since the completion of this series, I have seen one case of gravidity with absent Doederlein bacilli. This patient had a marked vaginitis.)

There were 26 fibroids:

Flora 1	0
Flora 2a without pus	10
Flora 2b with pus	3
Flora 3 without pus	9
Total	<hr/> 22
Flora 3 with pus (of these, three were obviously also inflammatory)	4
Total	<hr/> 26

There were 33 plasties:

Flora 1 (past menopause)	1
Flora 2a without pus	20
Flora 2b with pus	2
Flora 3 without pus	8
Total	<u>31</u>

Flora 3 with pus (of these, both had complete prolapses and protruding cervixes)

	<u>2</u>
Total	33

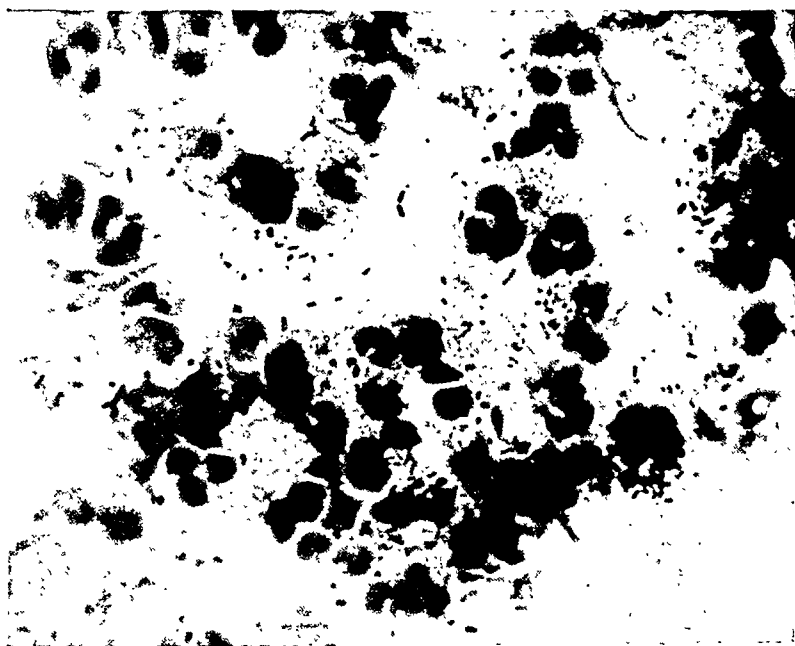


Fig. 6.—Flora 3b with pus, intra- and extracellular, gram-positive and gram-negative bacteria; no Doederlein bacilli.

There were 11 carcinomas of the cervix:

Flora 1	0
Flora 2	0
Flora 3 with pus	5
Débris, no bacteria	6
Total	<u>11</u>

There were 25 cases of diseased adnexa:

Flora 1	0
Flora 2a without pus	5
Flora 2b with pus	4
Flora 3 without pus	4
Flora 3 with pus	<u>12</u>
Total	25

There were 3 cases of tuberculous adnexitis:

Flora 1 (1 virgin)	2
(1 nullipara)	
Flora 3 with pus (this case also had a tuboovarian abscess)	1
	<hr/>
Total	3



Fig. 7.—Epithelial cells, occasional pus cell, debris, blood, no bacteria; a case of carcinoma of the cervix that had been treated by radium.

There were 12 cases of incomplete abortion:

Flora 1	2
Flora 2a without pus	3
Flora 2b with pus	2
Flora 3 without pus	2
Flora 3 with pus	3
	<hr/>
Total	12

#### CONCLUSIONS

A routine examination of vaginal smears correlated with the history is of some value in gynecologic diagnosis. The method is most useful in a differential diagnosis of gravidity, salpingitis vs. appendicitis, and diseased adnexa vs. neoplasm. The principal fact in the history to be taken into account is the number of births. The test is suggestive but in no sense pathognomonic.

# INTRAABDOMINAL REEFING OF THE PUBOCERVICAL FASCIA (MODIFIED POLK OPERATION) FOR THE CURE OF CYSTOCELE\*

By ROBERT T. FRANK, A.M., M.D., F.A.C.S., NEW YORK, N. Y.

(From the Gynecological Service of Mount Sinai Hospital)

DURING the last few years I have encountered a series of operative cases which caused me much thought and reflection. The first of these cases was a patient on whom an abdominal hysterectomy for fibroids had been performed by another operator, and in whom a complete evagination of the cervical stump and vaginal walls had taken place, which recurred again and again in spite of repeated operations. In another patient with cystocele, rectocele, and a large fibroid, I had performed an abdominal hysterectomy and ventrofixed the cervical stump to avoid such prolapse and eversion of the vagina. Although the stump remained fixed well up in the abdominal wall, a huge increase of the cystocele was soon noted. An attempt to cure the bladder prolapse by means of an anterior colporrhaphy from below was difficult and only partially successful.

In 1927 I was again confronted with a patient who harbored a large fibroma of the uterus and at the same time suffered from cystocele and rectocele. Preoperative examination showed that the vaginal walls were relaxed and that the cervix was movable. It thus became apparent that after hysterectomy the entire vault, including the cervical stump, would prolapse unless special measures to prevent this were taken. I therefore performed an abdominal supravaginal hysterectomy and double salpingo-oophorectomy, leaving as large an intraabdominal cervical stump as was feasible. After completion of this stage of the operation, I brought together the anterior vaginal planes beneath the bladder, by modification of the technic described by William Mecklinburg Polk in 1912, as part of an operation for prolapse. Having done this, I implanted the stump of the cervix, not covered with peritoneum, into the abdominal wall, according to the technic to be presently described. The result was excellent. Since then I have had the opportunity of using this same technic seven times under identical conditions.

In 1912 William Mecklinburg Polk of New York City, described an operation for procidentia uteri which, in the main, consisted in opening the abdomen suprapubically and shortening the sacrouterine and cardinal ligaments by means of a complicated suture passed

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\*Received for publication, June 1, 1929.

through the broad ligament. Neither the illustration nor the description of this suture has made its application understandable to me.

The portion of the operation that interests me and which I have repeatedly practiced with some modification, is the reefing and bringing together of the pubocervical fascia from within the abdomen. In the words of Dr. Polk:

"The peritoneal covering is now slit from the uterus to the bladder, the vagina being held taut upward. Through this opening (it may be enlarged by lateral incisions if necessary) the bladder is separated from the entire anterior face of the vagina as far as the urethra in extreme cases. This separation is made best with the gloved finger covered with gauze, or with gauze in a sponge holder, the grip of the gauze displacing the tissue with the least risk of injury to important structures. In this separation if one keeps to the vaginal wall, which is recognizable by its smooth and yellowish white structure, the ureters are pushed up and away from this canal, especially opposite the line which the first plicating suture must transfix. This line is as far down as possible upon the anterior surface of the vagina (about opposite the trigone). Seize the side of the vagina with a bullet forceps, taking a generous bite, draw it up and pass the suture from without in, repeat this on the opposite side from within out. In this fashion the vagina is plicated from below upward. The number of sutures required depends on the length of the vagina, rarely more than 4 are necessary; the arteries and veins are tied when necessary. Hemorrhage is rarely a troublesome feature and always easily controlled; rents in the cavity of the bladder are easily corrected, but need not occur."

Dr. Polk complicated his operation by tying the broad ligament sutures referred to previously and trusting to the insecure elevation produced, by plication, of the round ligaments, to hold up the uterus. He then excised or shortened the ridge resulting within the vagina by a small operative procedure from below. He reported 17 cases operated by this technic. This operative procedure has never become popular. One step, however, is of value.

Of the entire technic utilized by Polk, I have adopted in a modified form only that portion which applies to the reefing of the pubocervical fascia in the abdomen.

#### TECHNIC OF THE OPERATION

1. *Combined With Hysterectomy*.—In those cases in which large fibroids of the uterus exist coincidentally with cystocele and rectocele, the following technic has been used. Paramedian, suprapubic, transrectus incision; typical supravaginal hysterectomy, usually with bilateral salpingo-oophorectomy. In one case the adnexa of one side were retained. In amputating the uterus the stump must be left sufficiently long to permit of its ready fixation in the abdominal wall. This is tested by pulling the entire mass into the lower angle of the wound before the transverse section is performed.

The cervical or uterocervical stump is thoroughly cored out, so as to permit good approximation of the interior of the cervix, by means of several interrupted sutures. (See Fig. 1.) Careful tying of the uterine vessels and closure of the outer portions of the broad ligament with interrupted sutures is indicated because, as will be

seen hereafter, an unusual strain is put on the peritoneal covering of the pelvis. The cervical stump is pulled upward (cephalad) so as to tense the anterior structures.

The bladder is now gently freed downward toward the urethra and separated from the vagina, keeping strictly in the median line until the region of the

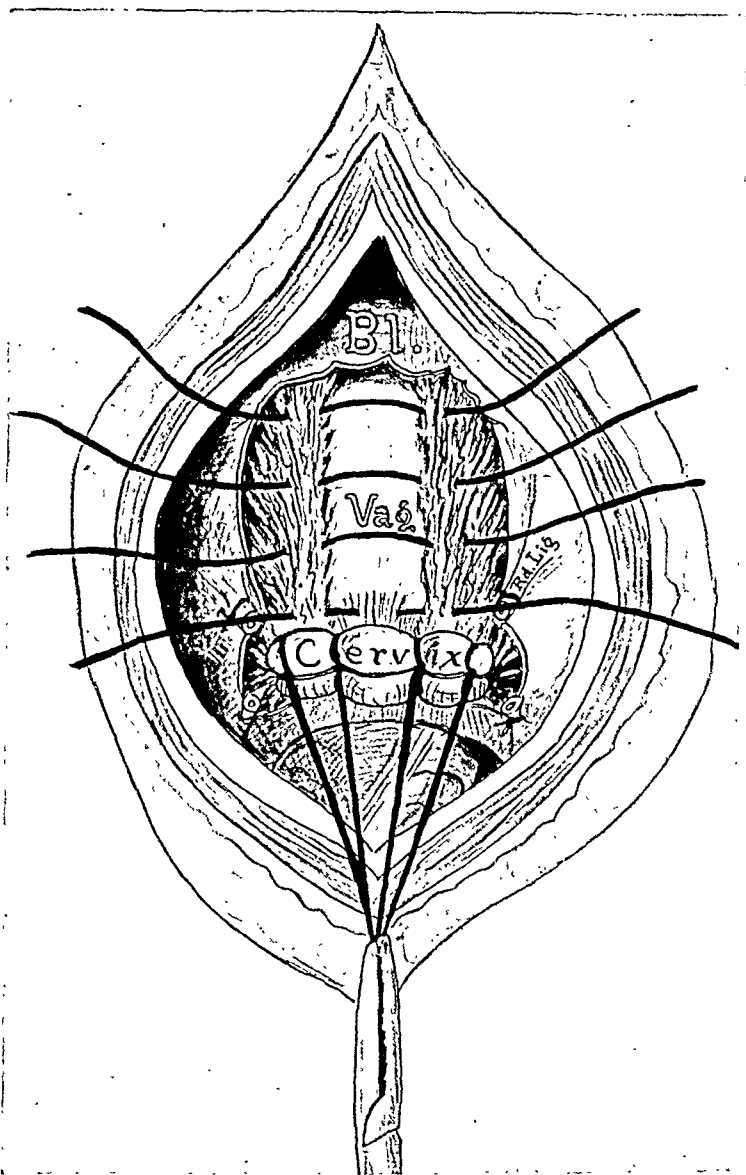


Fig. 1.—The cervical stump, after hysterectomy, is shown pulled cephalad. The bladder has been freed from the vagina. Four chromic sutures have been passed through the pubocervical fascia.

trigonum has been passed. The beginner with this operation can have an assistant pass a finger into the vagina from below in order that the distance from the introitus can be accurately gauged. It is important to separate vagina and bladder as delicately and bloodlessly as possible and this is best performed by first freeing in the median line. After this area has been liberated the bladder

may be separated laterally for one and one-half inches from the median line, care being taken not to injure the more or less developed, thin veins found in this region. A long, narrow retractor, wrapped with a few layers of gauze, is introduced to elevate the bladder toward the symphysis at the lower wound angle. The vaginal and cervical fascial planes are now readily visible if the patient is in steep Trendelenburg posture. Starting below the region of the trigonum a transverse suture is passed, taking in the pubocervical fascia on the patient's right side and crossing over the vagina and taking the left pubocervical fascial strands. Two other sutures are passed above the first one. The fourth suture includes the cervix of the uterus, approximately where the supravaginal and infravaginal por-

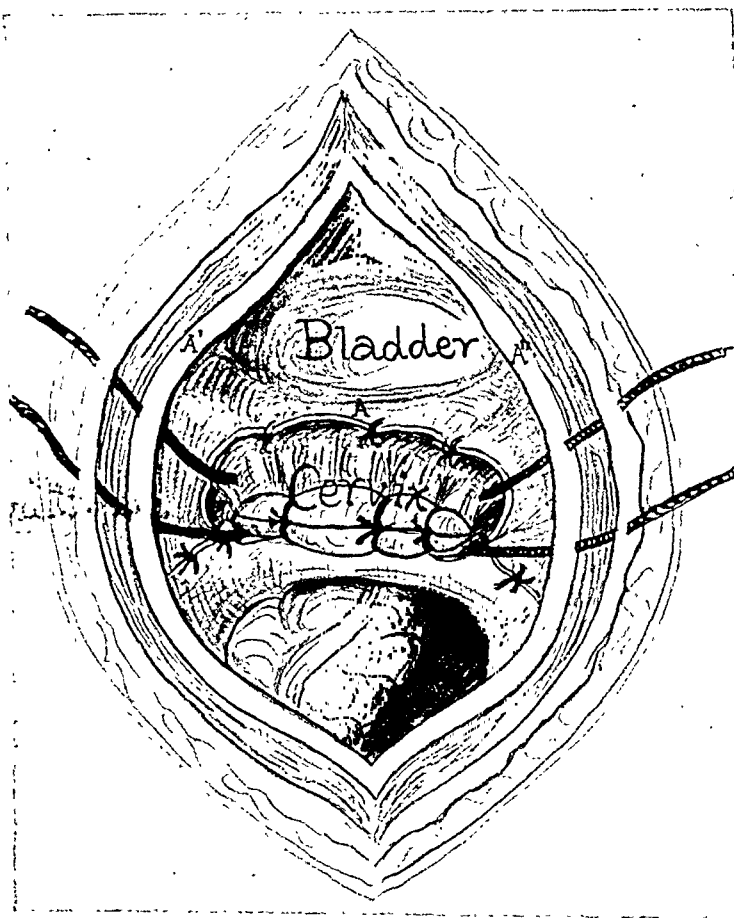


Fig. 2.—The anterior bladder peritoneum is shown sutured to the cervical stump and the broad ligament peritoneum is likewise closed. The cervical stump is not covered by peritoneum. Two heavy chromic ventrofixation sutures have been passed. During the peritoneal closure the three points A, A', and A'' are brought together by suture.

tions come together. Unlike Polk's directions, the sutures do not include the vagina. In order to prevent harm and infection resulting from accidental puncture of the vagina, I am in the habit of having the vagina disinfected beforehand by means of an acetone solution of mercurchrome. Starting from below upward, the chromic catgut sutures are tied. This brings the fascial layers together in the middle line.

The upper edge of the peritoneum reflected over the bladder is now sutured by means of the interrupted sutures about one inch below the upper region of the



cervical stump, anteriorly and laterally in the fashion shown in Fig. 2. This insures a large area of cervix denuded of peritoneum. The remainder of the peritoneal gap is closed as in every hysterectomy.

Ventrofixation sutures are now passed, starting on the right side. They penetrate the outer rectus sheath about one-half inch from the wound margin, next take in the peritoneum, and traverse the anterior extraperitoneal portion of the cervix from right to left. Emerging on the left side the suture passes through the left peritoneal

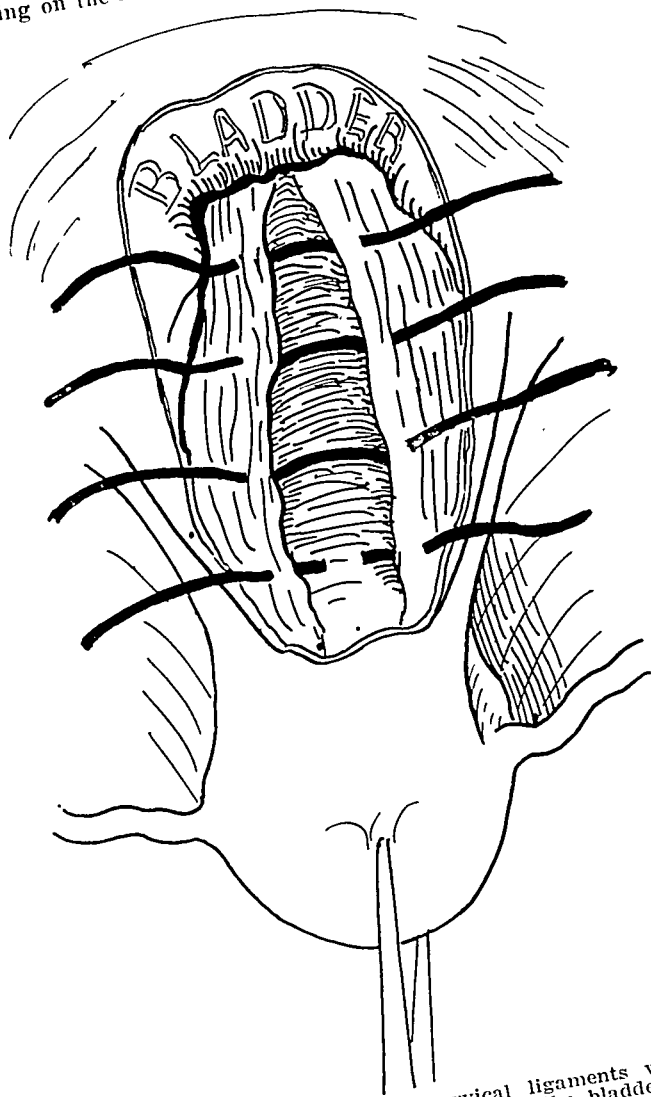


Fig. 3.—Intraabdominal reefing of pubocervical ligaments without hysterectomy. The uterovesical fold has been incised transversely; the bladder separated from the uterus and transverse sutures passed through the pubocervical fascia. The uppermost suture takes in cervical tissue.

edge and makes its exit through the rectus sheath on the left side. A second heavy chronic gut suture is similarly passed about one-half inch behind the first one. (Fig. 2.)

Peritoneal closure is effected by means of a peritoneal suture which includes the bladder peritoneum at its lower angle, and extraperitonealizes the entire uncovered cervical area. After complete closure of the peritoneum, the ventro-

fixation sutures are carefully tied, thus bringing cervical tissue in direct contact with the rectus sheath. The fascia and superficial tissues are closed by interrupted sutures in the usual fashion. A large packing is inserted in the vagina for two days in order to raise up the cervix and take off unnecessary strains from the ventrofixation sutures.

The results so far have been gratifying, the anterior vaginal wall being pulled up in a manner not obtainable by any operation performed from below, even when

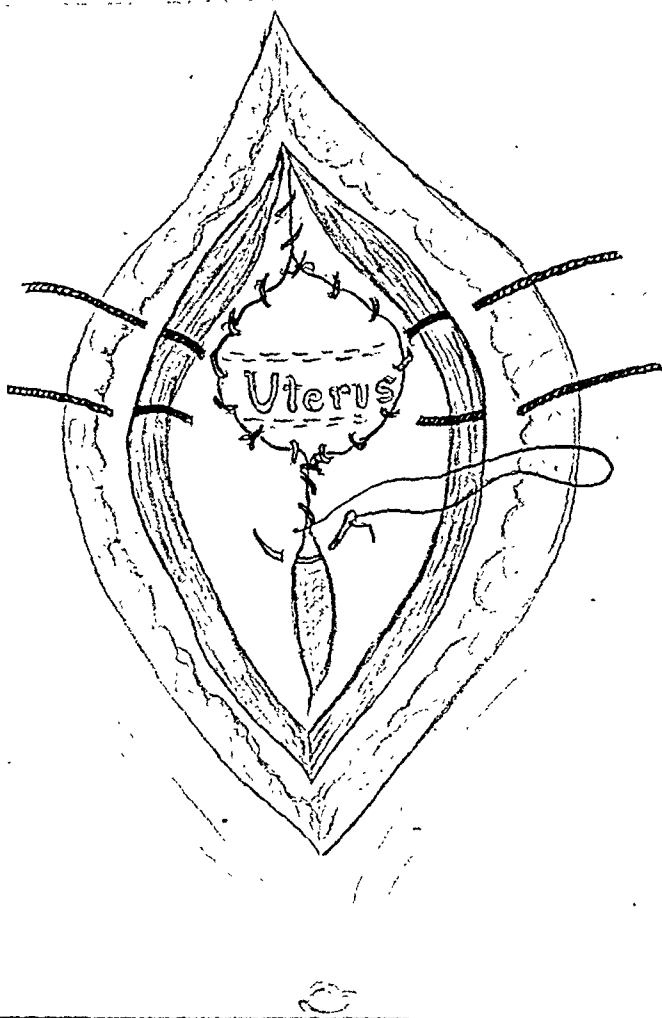


Fig. 4.—Ventrofixation with extraperitonealization of the uterine fundus. Shows peritoneum almost closed and ventrofixation sutures passed.

combined with ventrofixation of the stump. These results are in marked contrast to the case in which ventrofixation of the cervical stump after hysterectomy was unaccompanied by reefing of the fascial planes. Here an enlargement of the cystocele was noted.

2. *Without Hysterectomy.*—Encouraged by these results, I have enlarged the application of this technic to other conditions. The most recent indication has been a patient with recurring prolapse and cystocele who had been subjected to five previous operations from below, two combined with laparotomy. Although the large billiard ball cystocele appeared to be densely adherent to the anterior vaginal

wall and therefore much trouble was anticipated in separating vagina and bladder within the abdomen, I was pleasantly surprised by the ease with which this separation could be effected.

After opening the abdomen and cutting a three-inch, long, thin band uniting the uterus and abdominal wall, the sole remains of the previously performed ventrofixation (done by a different method than my own), the bladder peritoneum was incised from one round ligament to the other, and the uterus pulled backward and upward as shown in Fig. 3. The bladder was separated from the vaginal wall with surprising ease, to within a very short distance of the external meatus. By careful blunt dissection the fascial planes were exposed laterally without undue hemorrhage. The usual chronic gut sutures were passed as shown in Fig. 3, using a hemostatic needle as is always advisable. After these sutures were tied, the bladder was pulled upward and the peritoneum closed from round ligament to round ligament by interrupted sutures.

Thereupon the uterus was ventrofixed in the same fashion as the cervical stump (see Fig. 4), a technic somewhat modified from Kocher's extraperitoneal ventrofixation. By this technic, an area of the uterine fundus, fully the diameter of a 50 cent piece, is extraperitonealized and brought in direct contact with the rectus fascia. This is the type of ventrofixation that I regularly use in all conditions of prolapse.

I have been sufficiently encouraged by my results to now further extend the application of the modified Polk operation to other conditions.

At my suggestion, on my service this type of cystocele operation and ventrofixation was performed on a woman of seventy years with complete prolapse, under spinal anesthesia, the entire procedure occupying thirty-five minutes. If subsequently a perineorrhaphy is necessary, this will be done under parasacral anesthesia.

#### INDICATIONS FOR THE OPERATION

The technic of hysterectomy combined with reefing of the anterior fascia and extraperitonealization of the cervical stump is indicated in cases of fibromyomas uteri requiring abdominal hysterectomy in which there is a coincident cystocele and tendency to descent. This tendency to prolapse is frequently masked by a large uterus impinging on the pelvic brim which thus prevents the descent of the cervix and vaginal vault.

I propose to utilize this type of cystocele operation increasingly in all cases in which laparotomy is required for ventrofixation, in cases of rectocele, cystocele, and descent. Under these conditions a posterior colporrhaphy under parasacral anesthesia should be performed, the abdomen then opened, attending to the cystocele by the technic described, and completing the operation with ventrofixation.

Of the 7 patients operated upon, one patient who had a hysterectomy and fibroids with extraperitonealization of the stump, after an unusual afebrile convalescence of eleven days, died without warning on the eleventh day, from pulmonary embolus. Autopsy showed a typical large saddle thrombus occluding the two largest branches of

the pulmonary artery. The operative field had healed perfectly and there were no local thrombi to be found. Had the lethal outcome occurred with my first case, unquestionably I would have been frightened off from attempting further operations of this type. As, however, death from embolism occurs both after hysterectomy for fibromyomas of the uterus as well as in plastic operation with undue frequency, I consider this no reason to consider this more than the unavoidable tragic death from embolism to be occasionally expected.

The operation is technically not difficult if care be taken to avoid hemorrhage. If venous hemorrhage occurs, it can usually be checked by means of a carefully applied long artery forceps and ligation. Packing with dry gauze stops the venous oozing, which is further checked by approximation of the sutures. The ureters are in no danger if the sutures are passed, by sight, with the bladder well retracted, as the lower end of the ureter mobilizes with the trigonum and bladder. The contraindications to the operation are the presence of dense inflammatory exudates and adhesions which impair the mobility of the organs occupying the anterior portion of the pelvis.

NOTE: Since the writing of this paper, 9 additional patients were operated upon for cystocele, complicated by prolapse, rectocele, fibroid or dermoid cysts, by 4 different operators. The reefing of the pubocervical fascia, as described above, was done in conjunction with the extraperitoneal fixation of the uterus or cervical stump.

10 EAST EIGHTY-FIFTH STREET.

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## URETEROVAGINAL FISTULA SECONDARY TO A HIGH FORCEPS DELIVERY

BY RAYMOND E. WATKINS, M.D., PORTLAND, OREGON

(From the Department of Gynecology, University of Oregon Medical School,  
Portland, Oregon)

**I**NJURIES to the ureter occurring in the course of a pelvic operation are quite frequent. In the many reports of such accidents, the cause and prevention of these injuries, as well as the method of dealing with them, have been discussed. An injury to the ureter during labor, however, is extremely rare. One has to search carefully to find any definite record on this subject. Some authors of obstetrics mention that injuries of this type may occur, but with that they dismiss the subject. In a report on this type of injury by Judd,\* there were cited but two instances of ureterovaginal fistulas in which the injury was due to childbirth. Judd reports that in a large series of obstetric cases, Markoe had but one case at the New York Lying-In Hospital. In view of these facts I am sure the following case report will be of interest.

\*Collected Papers of Mayo Clinic, 8: 1916.

Mrs. A. M. I., married, aged twenty-four, consulted me on September 10, 1925, concerning a constant loss of urine. This condition began after a difficult labor, two and one-half months previously. The patient stated that she had pain in the region of the kidneys on both sides, which radiated around to the pelvis. She had had fever and chills nearly every day since the trouble began. Not all of the urine escaped, as the patient stated that she had voided two to four ounces of urine every two or three hours.

The patient was normal throughout her pregnancy and began labor at term on July 4, 1925. After twelve hours she was given an ether anesthetic and high forceps were applied. The delivery was very difficult, the patient being under an anesthetic about two and one-half hours. The baby was born dead. This delivery occurred in a small Oregon town and the patient was confined in her own home by a local physician. Following the delivery, she was unable to void and had to be catheterized for nearly a week. About this time she began to notice urine on her nightgown and the bed clothes. She remained in bed three weeks.

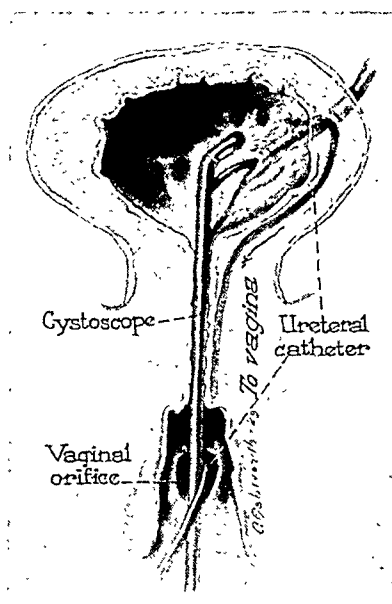


Fig 1.

When she was up and around again she began to have chills and fever nearly every day, which made her so ill that she was unable to carry on her duties about her home.

Her family history is unimportant. Menstruation began at twelve years of age, was of the twenty-eight day type, the flow lasted seven days and was rather profuse with occasional cramp-like pains. She did not have leucorrhea previous to pregnancy. No history of previous urinary disturbance. No symptoms referable to the gastrointestinal tract.

*Examination.*—The head, neck, chest, and cardiovascular system were negative. The abdomen was soft and flaccid. Palpation in the region of the right kidney and along the course of the right ureter showed moderate tenderness. There was considerable tenderness in the region of the midline of the abdomen just above the pubis. No masses or other pathology was found. Pelvic examination revealed a marked inflammatory condition of the vulva. There was a second degree perineal laceration well healed. The anterior vaginal wall was relaxed and

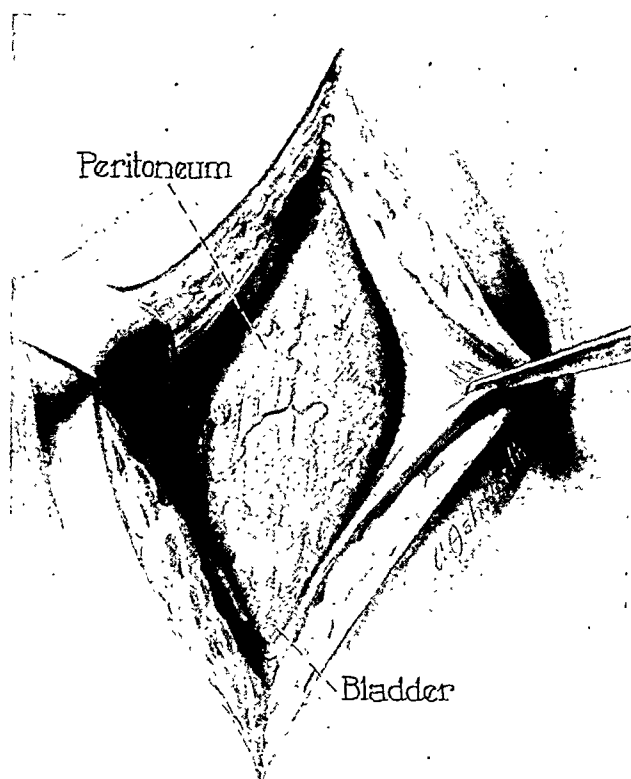


Fig. 2.

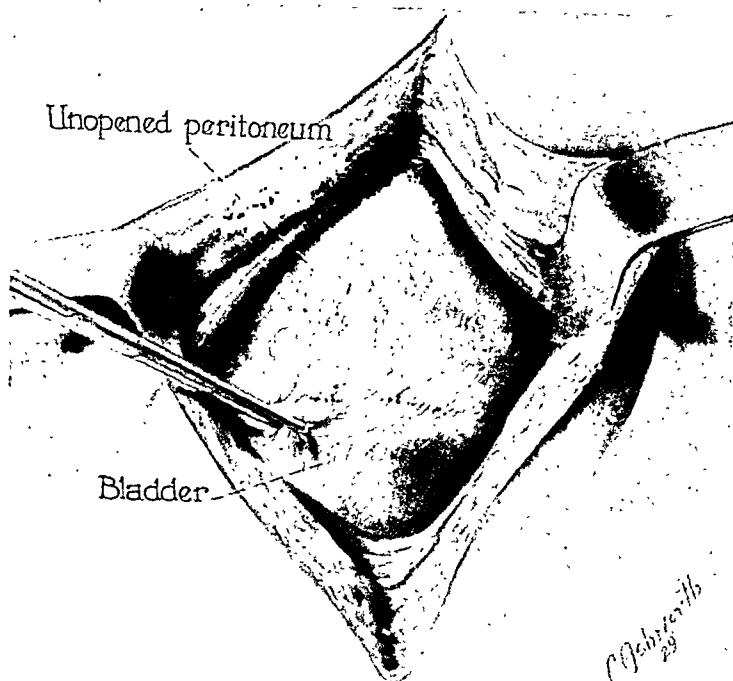


Fig. 3.

bulged moderately on straining. The cervix had a wide lateral laceration extending into the left vaginal vault and broad ligament. The uterus was in anterior position and of normal size. There was no evidence of a fistula in the anterior vaginal wall. The bladder was filled with boric solution and no leakage by vagina was observed.

An observation cystoscope was passed. Acute trigonitis was present, but the bladder was otherwise normal, there being no evidence of injury to the bladder walls. The following day a cystoscopic examination was made at the hospital to determine the condition of the kidneys and the ureters. The right ureteral catheter passed without difficulty; the left entered the ureteral orifice, and after passing about 3 cm. met an obstruction. On being forced it suddenly overcame the obstruction and passed freely but was found to have come out at the vaginal

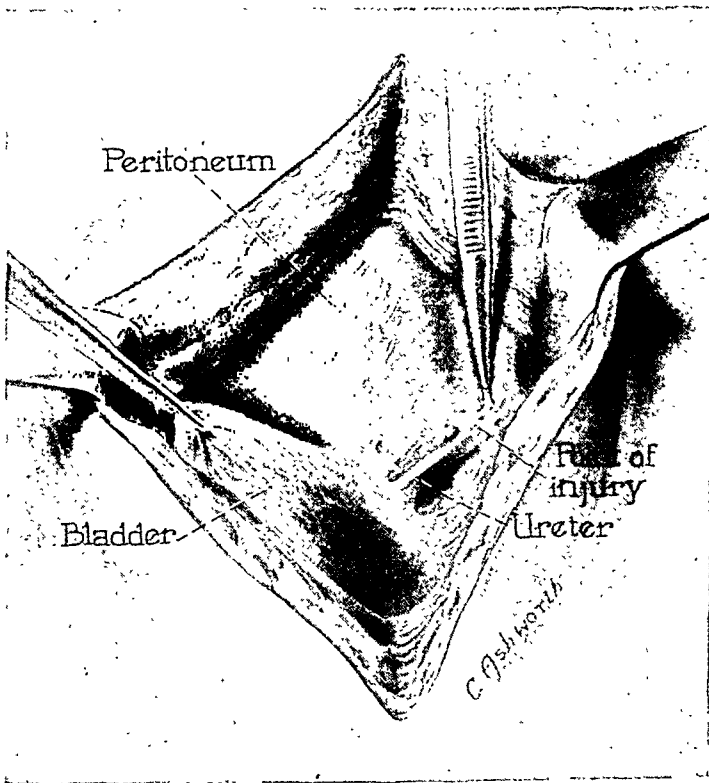


Fig. 4.

opening, thereby establishing the diagnosis of fistula of the left ureter at the point where the laceration of the cervix extended into the vaginal wall. (Fig. 1.) An attempt to pass a catheter through this opening up to the kidney was unsuccessful. The function of the right kidney was impaired and cultures of the urine showed a colon bacillus growth. The bladder culture revealed the same organism.

Upon admittance to the hospital this patient had an afternoon temperature ranging from 100° to 102° daily, which dropped to 99° in the morning. Her pulse was regular ranging from 90 to 110, with respirations of about 20. Her blood count showed a red count of 4,420,000, with hemoglobin of 75 per cent. There was a leucocytosis of 16,550 with 81 per cent polymorphonuclear leucocytes. The Wassermann was negative. Urine showed many pus cells, with an occasional blood cell.

On September 18, the day of operation, an attempt was made to locate the fistula vaginally with the idea of closure. This failed to expose it sufficiently, because of scar tissue and fixation high in the vault of the vagina. It was then decided to make a suprapubic incision and transplant the ureter into the bladder by the extraperitoneal operation described by Judd. On freeing the bladder from the front of the uterus and working laterally in the left wall of the pelvis (Figs. 2 and 3), it was found that the ureter was so bound down in a mass of adhesions that it could not be satisfactorily exposed (Fig. 4). An opening was made in the peritoneum and the ureter located where it passes over the bifurcation of the iliac vessels (Fig. 5). It was exposed from this point downward and freed

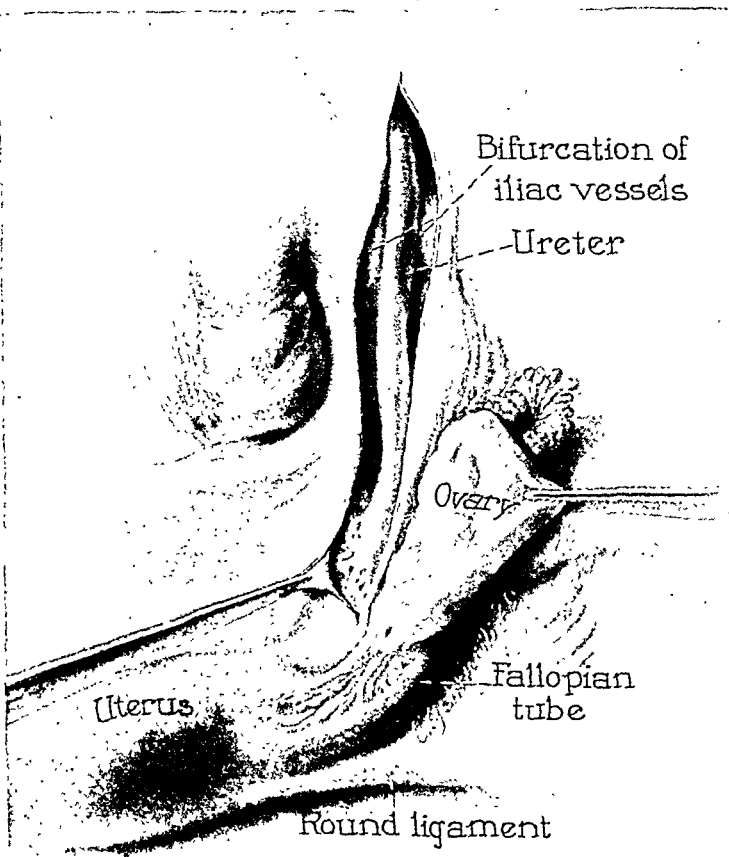


Fig. 5.

somewhat to a point where it seemed firmly fixed (Fig. 6). At this location the ureter was severed and the cut end transplanted through a small incision into the left lateral wall of the bladder (Fig. 7). The end of the ureter was split, the ureter pushed into the bladder, and the two ends stitched to the mucosa of the bladder (Fig. 7, *a* and *b*). The wall of the bladder was then carefully stitched around the ureter, making an inverted trough (Fig. 7, *c* and *d*). The adjacent perivesical tissue was tacked to the bladder in such a way as to prevent tension on the ureter. Fine chromic catgut was used. A rubber tissue drain was placed down to the side of the transplantation. The openings in the peritoneum were closed, and a cigarette drain was left in the abdomen in the middle of the wound.

Aside from a rather irregular temperature, which undoubtedly was due in a large measure to her pyelitis, the patient made an uneventful recovery. There was



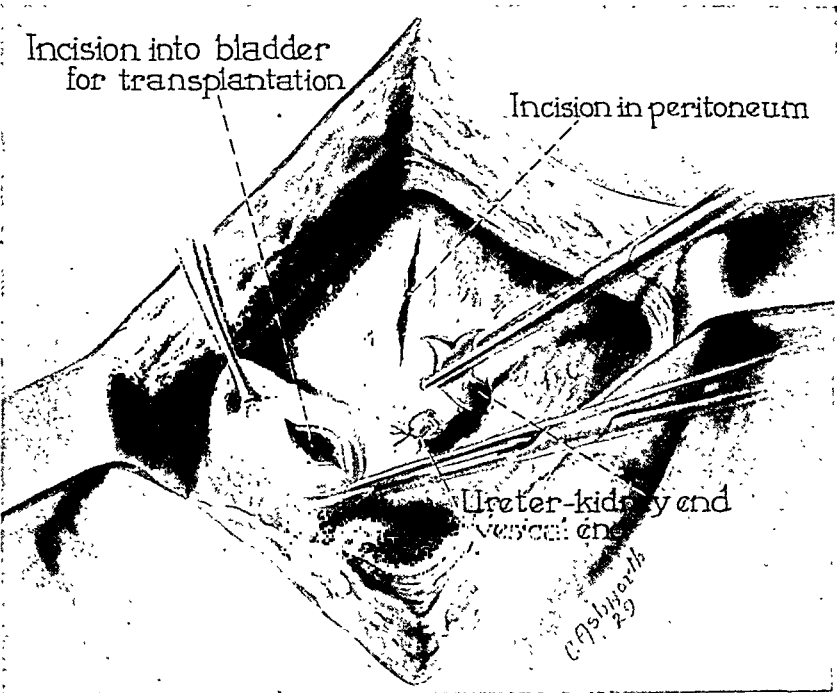


Fig. 6.

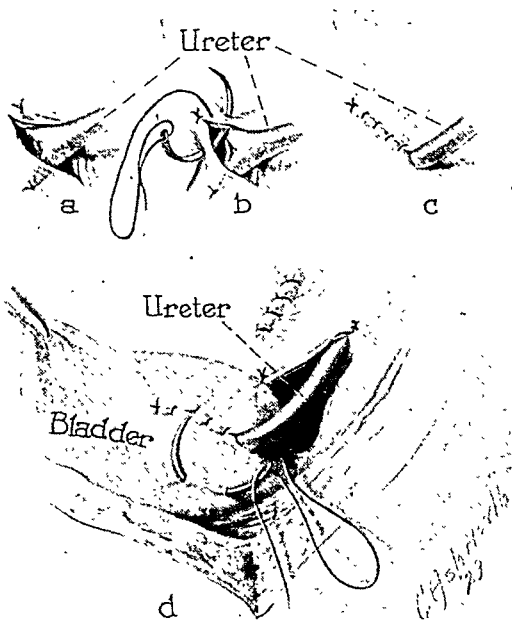


Fig. 7.

slight serous drainage from the abdominal incision for about three weeks, but this entirely cleared up and the wound closed. The patient left the hospital in good condition and returned to her home. Later a cystoscopy showed the new ureteral orifice, around which was a normal appearing bladder wall. Jets of urine could be seen coming through this opening at regular intervals. At the time the patient left the hospital she had full control of her bladder, and the vaginal leakage had ceased.

The subsequent history of this patient is interesting. August 23, 1926, she again consulted me, stating that she had not menstruated since May 12. Examination showed a pregnancy corresponding to the length of time she had missed her periods. Inasmuch as the cervix was firmly fixed high in the upper left vaginal vault, and with the history of a former very difficult labor and the above operation only a few months previously, much concern was felt about the outcome of this pregnancy. Her urine had never been free from pus since her first attack of pyelitis, which occurred shortly after the injury to the ureter. She had a justo-minor type of pelvis with a true conjugate of 10 cm.

The patient was kept under careful observation. In November she had an acute attack of pyelitis which lasted fifteen days. She then remained free from complications until January 1, when the bag of waters ruptured while she was riding on the train coming to Portland from her home about one hundred miles distant. On her arrival here she was sent to Emanuel Maternity Hospital and put to bed. She immediately went into labor and after eleven hours gave birth to a premature baby, weighing four pounds and nine ounces. Her convalescence was uncomplicated and she left the hospital on the fourteenth day in good condition. The baby was kept in the incubator and given mother's milk; it thrived from the beginning. A month later the baby weighed six pounds and was taken home.

Since the delivery, the mother has remained in good health and is able to care for her baby as well as do her housework. The infection of the urinary tract has resisted all types of treatment and still persists, but in mild form.

In the consideration of this case at the time of the operation, it was necessary to make a choice between ureteral transplantation and a nephrectomy. Since the opposite kidney was not only infected but the function impaired as well, a nephrectomy would have been attended with considerable risk. Ureteral transplantation into the bladder is a rational procedure and should be the method of choice in the hands of a competent surgeon.

## THE EFFECTS OF PREGNANCY ON BLOOD CIRCULATION IN THEIR RELATION TO SO-CALLED TOXEMIA

By J. C. BEKER, M.D., ARNHEM, HOLLAND

WE USE the term toxemia of pregnancy though we do not know specifically any substance that is responsible for this assumed intoxication. It seems to me entirely possible that such a toxin will never be found, since all the clinical phenomena typical of this condition can be explained by definite changes in the circulatory system during pregnancy.

I shall begin with a brief summary of alterations in blood circulation occurring during pregnancy under physiologic conditions.

The uterine wall becomes hypertrophied and included in this hypertrophy are both the arteries and veins. The growing uterus requires a larger supply of blood. More blood is carried to the uterus during pregnancy as result of such hypertrophic changes in the vessels which, according to Freund,<sup>1</sup> more than double the caliber of the arteries. Through them more blood flows to uterus and the surrounding tissues. This obviously is possible only in the presence of more blood. An increase in the total volume of blood by 10 to 15 per cent has been ascertained by Neubauer,<sup>2</sup> Mahnert,<sup>3</sup> and Stander.<sup>4</sup> Furthermore, there has been found, during pregnancy, an increase of the minute-volume output of the heart by about one-third as compared with the nonpregnant woman by the investigations of Weiss,<sup>5</sup> Stander and Duncan.<sup>6</sup> About two to three weeks after delivery this minute-volume output again had returned to normal. These observations were fully confirmed by the work of Frey.<sup>7</sup> He observed this increase in heart output in the majority of cases within the first half of pregnancy. As early as the fourth month of pregnancy, he ascertained an increase of the heart both in its longitudinal and transverse diameters.

Investigations of Hinselmann,<sup>8</sup> and Nevermann<sup>9</sup> carried out with the capillary microscope showed that in normal pregnant women stases in the capillary flow occur approximately four times as frequently as in nonpregnant individuals.

The quantity of blood supplied to the pregnant uterus through uterine and spermatic arteries, however, also depends upon the pressure prevailing in the general circulatory system. It would be erroneous to explain the increased supply in response to the increased demand solely on the basis of the widening of the afferent vessels.

Hess<sup>10</sup> has made it convincingly clear that the deciding factor in the proper supply of blood to any organ is found in the total resistance to the flow offered by all end ramifications in the vascular area. Therefore, a physiologically normal supply of blood for the pregnant uterus

calls not only for a widening of the vessels but as well is dependent upon the absence of any abnormal regional resistance to the blood flow, that is, chiefly within the uterine wall. With a normally growing ovum within a normally hypertrophying uterine wall, there will be no increased resistance and thus no noteworthy effect on general circulation.

Under normal conditions the circulatory system seemingly adapts itself satisfactorily to altered demands by an increase in the total amount of blood, by an enlarged minute-volume output and by a certain amount of peripheral vasoconstriction to maintain a proper level of blood pressure.

Some change is brought into the situation by the onset of labor and probably even in the last stages of pregnancy by frequent contractions of the uterus. Every uterine contraction obviously must increase the resistance offered to the blood flow. And after each contraction there must be a freer inflow of blood in order to maintain a sufficient blood supply in the intervillous spaces.

Compensation for this increased resistance during contractions must be furnished by general circulation. Fellner<sup>11</sup> ascertained an increase in the heart output and in blood pressure with the beginning of labor. Peripherally observed, the number of stases in the capillary stream increases in the first phases of labor by 18 per cent, and in the second stage by 28.5 per cent (Hinselmann).

In my opinion, these compensating, favorable reactions in the general circulatory system are induced by the augmentation of regional resistance in the uterus and required for securing an adequate blood supply for the fetus during and after uterine contraction.

It seems likely that vasoconstriction, easily noticed in peripheral arterioles, also occurs, and thus asserts its influence, in other organs, especially in the kidneys. An insufficient supply of arterial blood in them possibly results in the appearance of albuminuria (Lichtwitz<sup>12</sup>). During labor the urine commonly is found to contain albumin and even casts.

Parturition, it is my belief, often pushes the function of the circulatory system to its physiologic limits. We have seen that to pass through pregnancy and labor within such limits the following conditions must be fulfilled: (1) The heart must be capable of enlarging its minute-volume output; (2) peripheral arterioles must undergo a certain degree of constriction; (3) the arteries of the uterus must adequately hypertrophy; and (4) the uterine muscle must remain in a state of tension which does not offer an abnormal resistance to blood flow.

Complications, therefore, might arise from any of the four mentioned and requisite conditions.

(1) A disturbance in required cardiac function is to be expected if a heart lesion antedating impregnation already has required an increased minute-volume output to prevent decompensation. This holds

particularly true for an aortic stenosis, since here further increase of the minute-volume could be obtained only with evident difficulty.

During pregnancy particular attention is required for women in whom a constitutional hypoplasia of the arterial system is responsible for subarterialization of certain organs.

(2) Difficulties in the peripheral circulation can be expected in women in whom such conditions as essential hypertension or a chronic nephritis have already, before impregnation, increased the demands on the



Fig. 1.—Primiparous cow, two months pregnant in left horn.

circulatory system. Even with pregnancy itself progressing normally further requirements on necessary vasoconstriction may seriously affect circulation in other organs. In this manner might be satisfactorily explained a pregnancy nephritis and eclamptic convulsions in older multiparae who have safely passed through preceding pregnancies.

(3) Considering next insufficient hypertrophy of uterine vessels, we must remember the evident anatomic differences between the uterus of a primiparous and that of a multiparous woman. Unable to secure for demonstration of this difference human uteri I injected, after the method

of Gross,<sup>13</sup> the arteries of uteri of cows with barium gelatin and took x-ray pictures. The illustrations here shown (Figs. 1 and 2) represent the uteri of cows, both two months pregnant, the one a primigravida, the other a multipara. In the multiparous animal the uterine wall is thicker and its arteries of a markedly larger caliber.

(4) Obviously the development of the blood vessels in pregnancy is closely related to the hypertrophic development of the myometrium. Therefore, the same difference between a primiparous and a multiparous uterus will exist in regard to uterine wall that was pointed out above in regard to uterine vessels. Less additional hypertrophic growth of the muscle will be required in the multiparous organ to attain competent functional ability, decidedly more in the uterus of the primigravida.

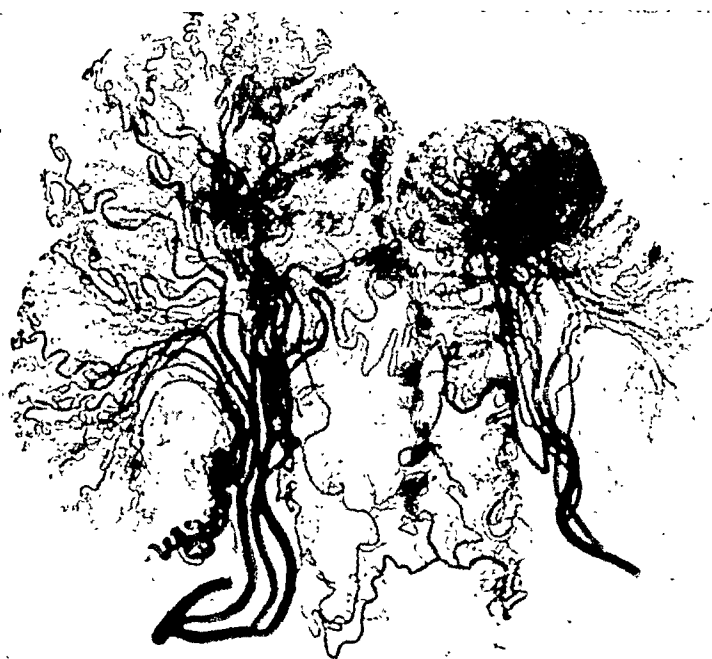


Fig. 2.—Multiparous cow, two months pregnant in left horn.

I have pointed out how during a uterine contraction resistance to blood flow is increased, and this resistance must be overcome by a rise in general blood pressure. But also between contractions the required increase of afflux of arterial blood into the intravillous spaces is dependent on a normal tonus of the uterine wall. In a previous paper<sup>14</sup> I have explained how the tonus of the uterine muscle changes under the influence of the uterine contents. It must be assumed that under normal conditions this change in tonicity will be such as to guarantee a sufficient blood supply for the fetus in spite of contractions late in pregnancy or during labor.

It seems logical that too high a tonus of the uterine muscle might result either from a deficient muscle hypertrophy or from the impos-

sibility of adequately prompt hypertrophy on account of unduly rapid increase in the size of the uterine contents. This first form of actual deficiency then is most likely to obtain in the primigravida, and the second form of relative deficiency prone to occur in cases of multiple pregnancy, of hydramnion or of placental ablation with copious hemorrhage.

Abnormally high tonicity of the uterine wall means abnormally high resistance in a part of the circulatory system. As protective and remedial reactions then must be expected a rise of general blood pressure which is achieved by increase of the cardiac output, and vasoconstriction in peripheral areas and within certain organs.

In comparison to the intermittent and only temporary interference with blood flow through the uterine wall during labor, the abnormally high tonicity of the insufficiently developed or of the abnormally distended uterine wall during the latter part of pregnancy represents a chronic and long persisting condition. Thus the aforementioned reactive and protective changes in general circulation will be persisting. The rise in blood pressure will continue. Very frequently interrupted capillary flow will reduce blood flow through certain organs to a degree not any longer compatible with their anatomic and functional integrity. I believe that in this manner are satisfactorily explained such clinical phenomena and pathologic findings as hypertension, albuminuria and evidences of anatomic damage in kidneys or liver. From the foregoing it seems obvious why these disturbances, termed toxemia, as a matter of fact are observed so much more frequently in the primigravida or in the course of a multiple pregnancy.

We should differentiate between two forms of "toxemia." The one due to this abnormal resistance offered to blood circulation within the uterine wall, and another the result of insufficient heart action or insufficient blood supply to certain organs on account of impaired peripheral circulation.

The accepted symptoms of toxemia appear five times as often in cases of multiple pregnancy as compared with their incidence in single pregnancy. In instances of rapidly growing hydatid mole or hydramnion a kidney disorder is frequently encountered. Also the clinical signs of toxemia in connection with ablatio placentae might be explained on the basis of abnormal tension of the uterine wall.

What will be the reaction of general circulation to accomplished delivery?

Frey noticed that within fifteen minutes after delivery the minute-volume decreased from 10.4 to 8.4. In regard to peripheral vasoconstriction, Hinselmann observed that stases amount in the second stage of labor to 28 per cent, but one hour postpartum to only 8 per cent, after twenty-four hours to 6 per cent, two to five days postpartum to only 2.4 per cent. As a rule the urinary output quickly increases and albumin gradually disappears. During normal delivery blood pressure usually

risers 10 to 20 mm. Hg. (Vignes,<sup>15</sup> Schwarz<sup>16</sup>) and often returns to its previous level within ten minutes after delivery. After a normal delivery the general circulation will have attained normal conditions within a few hours.

When during pregnancy or labor the symptoms of so-called "toxemia" are evident the various pathologic phenomena disappear more slowly.

The uterus of a "toxic" patient usually contracts promptly and often reduces the actual blood loss below normal. Thus often the total quantity of blood retained within the circulatory system will remain relatively large and this fact in itself is prone to interfere with speedy return to normal conditions. The arterial hypertension as a rule decreases after delivery but not always. In some instances the fall is sudden and great, up to 100 mm. (Schwarz), in many others the decrease ensues very slowly. De Snoo<sup>17</sup> points to the important fact that the abnormally high blood pressure will in many cases fall only to rise again afterward. Hinselmann definitely ascertained that in the toxemic patients the number of stases will not decrease for some time. It seems probable that this process of restoration is greatly dependent upon the extent and degree of pathologic tissue changes and whether regeneration is quickly or at all possible.

On the other hand, we certainly see cases of hypertension, caused by increased minute-volume cardiac output and excessive peripheral vasoconstriction, in which the reaction is so sharp, and sudden widening of constricted arterioles results in so sudden and deep a drop in blood pressure that the heart cannot respond with sufficient promptness. If not properly managed these patients will die in shock. There cannot be any doubt that in cases of marked hypertension the danger to the patient is by far greater immediately after delivery than it had been before.

#### CONCLUSIONS

The normal changes of general circulation during pregnancy, labor and the puerperium are of great significance.

Resistance to blood flow through the normal wall of the pregnant uterus does affect general circulation in a definite manner.

When this uterine resistance becomes abnormally large, and especially in an individual whose circulatory system is incapable to compensate fully for even only the physiologic increase in resistance, the development of certain pathologic conditions, usually ascribed to a toxemia, becomes almost inevitable.

In these patients, in the presence of marked hypertension, great danger arises when the circulatory system does not adjust itself promptly to the change of conditions brought about by delivery.

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## A THEORETICAL CONSIDERATION OF THE ETIOLOGY OF THE TOXEMIAS OF PREGNANCY

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(Clinical Assistant in Gynecology, Northwestern University Medical School, Chicago)

THERE are two great methods of reasoning, the inductive and the deductive. Making deductions from an established premise may be the safer method but induction of a conclusion from a number of facts is the more fascinating. While inductive conclusions often require confirmation, their promulgation may be productive of important knowledge.

Deductive methods have failed to clear up the question of the etiology of the toxemias of pregnancy. However, a great amount of work has been done in the endeavor and a certain number of facts have been established. Among these is the fact that a carbohydrate depletion and an acidosis (or hypoalkalinity) exist in the persons afflicted with such a toxemia and that they are benefited by the administration of glucose and alkalis. But though the fact exists the reason for its existence is not apparent. Many theories have been advanced. None suffice.

Anyone who is interested in obstetrics has given thought to this question. After the failures of many careful and capable investigators, the solution has not appeared hopeful. The stimulus for the theory we herein discuss came from an article on the "Newer Aspects of Liver Disease" by Andrews, Thomas and Schlegel.<sup>1</sup> While their paper did not carry a suggestion of the applicability of their findings to the conditions we are considering, it appears to us that they may have an important bearing on them.

It has been shown by many investigators that the permeability of cells is dependent upon and varies with the mineral salt content of the cells. To support the life of the cell a very delicate balance of the calcium ions on the one side and the sodium and potassium ions on the other must be maintained. An excess of calcium ions causes lessened permeability which may progress to the point of absolute impermeability and consequent loss of the power of absorption and excretion through its cell membrane. An excess of potassium or sodium causes an increase of the permeability of the cell which may progress to the point of dissolution of the cell through its own membrane.

Mason and his coworkers,<sup>2</sup> a few years ago, demonstrated that if small amounts of liver were removed and dropped back into a dog's abdomen a toxemia ensued which was rapidly fatal. Death within eighteen to twenty-four hours resulted from using only a few grams of liver in this way. These experiments were criticized as having probably caused death by peritonitis. To check them, Andrews and his coworkers repeated the procedure but inserted the liver fragments into the chest and axilla. The results were the same. The assumption that death was due to a liver protein poisoning was inevitable. With these and other facts in mind Andrews, Thomas and Schlegel undertook their study. They state, "It is obvious, therefore, that there is a substance in the liver which can cause severe toxemias. . . ."

These investigators then produced artificial hepatic disease by tying the common bile ducts in some dogs and by causing ether toxemia in others. A study of each dog's urine and of the mineral salt content of normal and pathologic dog livers was made. In both types of liver disease produced, early specimens of urine showed a protein which reacted to antisera which were sensitive to dog livers and did not react to antisera sensitive to dog blood. From this they concluded that the urinary protein positively originated in the liver. Their study of the mineral salt content of the pathologic livers showed a marked decrease in calcium, only a slight variation in potassium, and an enormous increase in sodium. Such an imbalance of the mineral salt ions would account for the dissolution of the cells which a microscopic examination showed to have taken place. They conclude that, in all probability, the protein found in the urine is leakage from the liver cells due to their greatly increased permeability following the disturbance of the mineral salt balance.

How may these findings be applied to a solution of the etiology of the toxemias of pregnancy?

Are hyperemesis gravidarum and eclampsia two distinct conditions with independent pathologic bases and of different etiology? Their clinical manifestations have enough in common to stamp them as closely related conditions. Hyperemesis usually occurs in the first trimester and eclampsia in the last. Practically never do both occur in the same pregnancy. We are inclined to believe that eclampsia is a manifestation of an accumulative action of the same causative factors involved in the etiology of hyperemesis but occurring in those women who have been able to withstand the invasion in the early months. The final breaking down of this resistance results in the storm of symptoms known as eclampsia rather than in the milder condition of hyperemesis. Thus it would be possible to have the same etiologic basis for both.

The developing fetus is a parasite, preying upon its parent for existence. That there is an unusual demand for calcium is evidenced by

the pathologic changes that sometimes take place in a pregnant woman, such as osseous changes and caries of the teeth. It has been estimated that a fetus may withdraw as much as 100 gm. of calcium from its host, during the process of gestation. If the withdrawn calcium is not replaced through a proper diet or, if it be ingested but not metabolized, it is not difficult to conceive of an imbalance of minerals in the liver cells resulting and with this an increase in the permeability of these cells. There will follow an outpouring of the glycogen stored there, with a consequent depletion of carbohydrates. As is well known to physiologists and pathologists, an organ which becomes deficient in the performance of its function will oftentimes make extraordinary efforts to compensate and thereby sometimes function pathologically. In the presence of an increased permeability of its cell membranes, the liver cells, having depleted themselves of their glycogen stores, in a vain endeavor to compensate, will secrete into the system certain toxic proteins which would never pass through the membranes of cells with normal permeability. The resulting toxemia would manifest itself, in the early months of pregnancy, either as the ordinary vomiting of pregnancy or, if adjustment to conditions did not soon take place, as hyperemesis. In the later months, due to cumulative action of the toxic material, those who had resisted the early invasion of these toxins, but who had not actually adjusted themselves to the altered conditions, would suddenly be overwhelmed and manifest the defeat by the condition known as eclampsia.

The blood does not show any characteristic changes as to mineral content, either in normal pregnancy or in the toxemias. We have run a small series of blood examinations during pregnancy and were unable to demonstrate any abnormalities in the ratio of calcium against sodium and potassium. This does not, however, eliminate the possibility of an imbalance existing in the liver cells as was demonstrated by Andrews and his coworkers.

A consideration of the matter of calcium deficiency involves more than a regulation of calcium intake as the condition may exist in the presence of an abundance of calcium ingestion unless it is metabolized.

Pregnancy places a strain on all the body functions. That the endocrine system may suffer is shown when pregnancy occurs in a woman suffering from hyperthyroidism. It is thought that the parathyroid glands, either alone or in conjunction with the thyroid, govern calcium metabolism and that they serve to neutralize toxic wastes and contribute toward the maintenance of blood alkalinity. If the thyroid gland suffers and sometimes breaks under the strain of pregnancy why may not the parathyroids suffer and likewise break? If the functions attributed to these glands are correct their failure will establish a vicious train of events. First, the deficient calcium metabolism may cause an imbalance of mineral salt content and an increase in the per-

meability of the liver cells. A carbohydrate depletion then ensues. In their desperate efforts to secrete, the liver cells pour out their own toxic proteins. This process may progress to the point of dissolution of the cells as seen in sections of eclamptic livers. Normally, toxic wastes are neutralized by the parathyroids but now, in their impaired state, they are unable to accomplish this. They fail to control a situation brought about by their own deficiency.

If this theory has any merit, the treatment will suggest itself. Prophylaxis will, of course, be of greatest import. If it be a matter of mere insufficiency of calcium intake, an abundance of calcium salts taken by mouth may prove effective. None are easily assimilable though the lactate is perhaps best. If it be a matter of deficiency of calcium metabolism in spite of sufficient intake, the administration of an extract of parathyroid gland may be indicated. Parathormone appears to be an efficient preparation. The early routine use of this procedure may be of value as a prophylactic measure. In the active treatment, the present use of glucose and alkalis may be supplemented by the use of calcium and parathormone.

In the active treatment of eclampsia, magnesium sulphate has attained an important position. The value of this salt, when injected parenterally, is supposed to lie in its own sedative property and its synergistic action when combined with morphine. If our theory as to the etiology of the toxemias of pregnancy is correct, it is quite likely that the favorable action of magnesium sulphate may have a deeper significance.

Mendel and Benedict<sup>3</sup> have shown in their work that "the increased excretion of calcium is accompanied by a rise in the urinary output of magnesium." They further state that "the injection of either calcium or magnesium brings about the presence of an increased amount of either metal in the blood" which, they suggest, is "an antitoxic compensatory response of the organism whereby the toxic action of the injected metal is, to some extent, overcome."

In other words, calcium and magnesium, in the human physiology, are compensatory and complementary to each other. They are, in a sense, antagonists and the increase of one stimulates an increase in the other as a safeguard against possible toxicity. If this be true, may it not also be true that the injection of magnesium sulphate in eclampsia causes the body to draw upon its available calcium thus raising the calcium content of its cells? If the toxemia is due to an imbalance of the mineral content of the liver cells (calcium deficiency) with a consequent increased permeability of these cells and an outpouring of their toxic proteins, then the injection of magnesium with its accompanying rise in the calcium level will tend to alleviate the condition by normalizing the mineral ratio between calcium and sodium and potas-

sium. The permeability of the cells will be reduced to the normal state and the secretion, into the organism, of their toxic contents will be inhibited.

In rachitis the metabolism of calcium is intimately associated with that of phosphorus. A partial examination of the literature shows a general agreement in the opinion that rachitis is accompanied by a deficiency of both calcium and phosphorus and that each of these elements are essential in the treatment. Sittler<sup>4</sup> gives a combination of nucleinic acid with calcium glycerophosphate. Huenekens<sup>5</sup> uses tricalcium phosphate. Orr, Holt, Wilkins, and Boone<sup>6</sup> state that rachitis is due to the failure to *retain* calcium and phosphorus. They also show that irradiation of the patient with ultraviolet rays causes a large amount of calcium and phosphorus to be retained. Others have shown that irradiation of certain oils with ultraviolet rays gives these oils antirachitic properties. These observations may explain the specific action of cod liver oil in rickets in that it causes the body to retain calcium and phosphorus.

Because of the interdependence of these two elements in rickets, it would be of interest to know if the presence of phosphorus, which is found in nearly all the body cells, is essential to the metabolism of calcium. If so, it would assume an important position in our theoretical consideration of the etiology of the toxemias of pregnancy. Furthermore, if exposure of the body to ultraviolet rays causes a retention of its calcium and phosphorus and if our theory is correct, irradiation with ultraviolet rays would have a place in the treatment of these toxemias.

We venture to predict that a further investigation of the calcium, phosphorus, and magnesium metabolism, with their possible interrelationship and interdependence, may clear up, at least in part, the etiology of the toxemias of pregnancy and may provide a means of preventing and treating the conditons.

As stated in the title of this paper our discussion is a purely theoretical one, an endeavor to explain a vexing question through inductive reasoning. If the theory has been advanced before, we are not aware of it. If it stimulates others to experimentally confirm or refute it, it will have served its purpose.

We wish to express a real appreciation to Miss A. A. Jansen, Director of the North Shore Clinical Laboratory, for helpful information and suggestions concerning the mineral content of the blood and for the chemical examination of a series of blood specimens from pregnant women.

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## THE DIAGNOSIS OF ECTOPIC GESTATION\*

FROM A CLINICAL ANALYSIS OF 410 CASES AT BELLEVUE HOSPITAL

By THOMAS E. LAVELL, M.D., F.A.C.S., NEW YORK, N. Y.

ECTOPIC gestation has received much attention in medical literature but remains of peculiar interest, not only because of its potentially tragic course but because of the constantly high rate of diagnostic error.

Notwithstanding all that has been learned, there still remain several features which are not satisfactorily settled. The baffling problem of diagnosis in particular presents a continual challenge which has not been adequately answered. Toward this phase the present paper is directed in the hope that by surveying a large group of cases, we may approach a more accurate evaluation of detail and a consequent truer perspective.

### EXPLANATION OF THE SERIES

The following study includes the ectopic pregnancies treated on the Gynecologic Service at Bellevue Hospital during a period of seventeen years. The series is consecutive and represents all available cases since the start of the new Bellevue record system.

Recognizing that pelvic hemorrhage is sometimes due to conditions other than ectopic pregnancy, only cases with pathologic or operative verification were considered. Four hundred and six were operated upon and 4 others demonstrated by autopsy. Many histories were incomplete in certain details, so percentages were necessarily limited to the number mentioning that detail. The charts are arranged with a view to emphasis of exceptional as well as common conditions, as this knowledge is of great value at times in doubtful cases. Indefinite statements together with equivocal diagnoses were discarded. It is to be remembered that this represents a group with symptoms and pathology advanced enough to bring them into a hospital, often in serious condition. There is therefore a disproportionate absence of early cases preceding tubal rupture or abortion.

### GENERAL CONSIDERATIONS

Age incidence ranged throughout the entire childbearing period, with a notable concentration between twenty-five and twenty-nine years. Race, as well as nativity, apparently followed that of the general hospital population, though this could not be verified. There were 176 white and 24 black patients. Histories were usually obtained by in-

\*Read, by invitation, before the New York Obstetrical Society, March 12, 1929.

ternes or student clerks and later checked by attending staff. Length of time in hospital before operation may be taken as a gauge of diagnostic difficulty.

About 50 per cent were operated upon within twenty-four hours after admission, while the remainder required a more or less prolonged period of observation to establish a diagnosis.

#### HISTORY OF PELVIC INFLAMMATION

Although there was a surprising lack of history of pelvic inflammation, puerperal or venereal, that had been treated palliatively at home or in the hospital, there was a very large number of women (26.8 per cent) who had had previous operations on the pelvic organs. The

### PAST HISTORY-OPERATIONS ON PELVIC ORGANS WOMEN WITH ECTOPIC PREGNANCIES

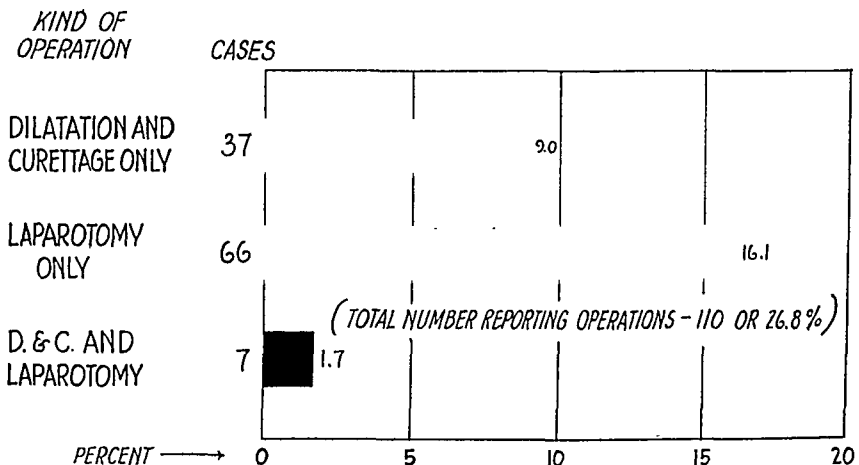


Fig. 1.

inference may be drawn that the pathology was of mild type, not enough to cause sterility and suitable for more or less conservative surgery. We cannot escape the possibility also that the operation itself may have been a damaging factor which predisposed to later ectopic gestation. (Fig. 1.)\*

#### PREVIOUS PREGNANCIES

The average number of previous pregnancies was 2.8, and of children born was 2.3. This record of childbearing would compare very favorably with that of any cross-section of the married female population of this age group. As the number of abortions was relatively

\*I am greatly indebted to Mr. Herbert Marks of the Statistical Department of the Metropolitan Life Insurance Co. for assistance and advice in the preparation of the accompanying charts.

small, it is probable that abortion is of little importance as a causative factor. No increased incidence of puerperal complications was noted. (Fig. 2.)

## NUMBER OF PREVIOUS PREGNANCIES OF WOMEN WITH ECTOPIC PREGNANCIES

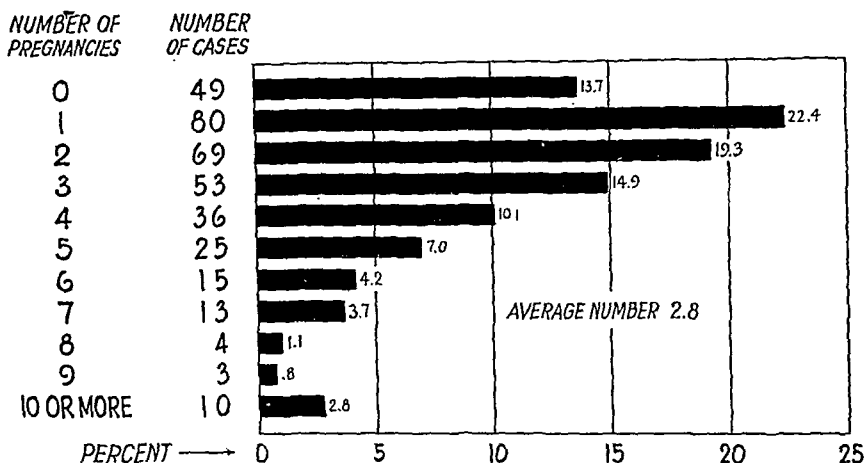


Fig. 2.

## TERMINATION OF PREVIOUS PREGNANCIES OF WOMEN WITH ECTOPIC PREGNANCIES

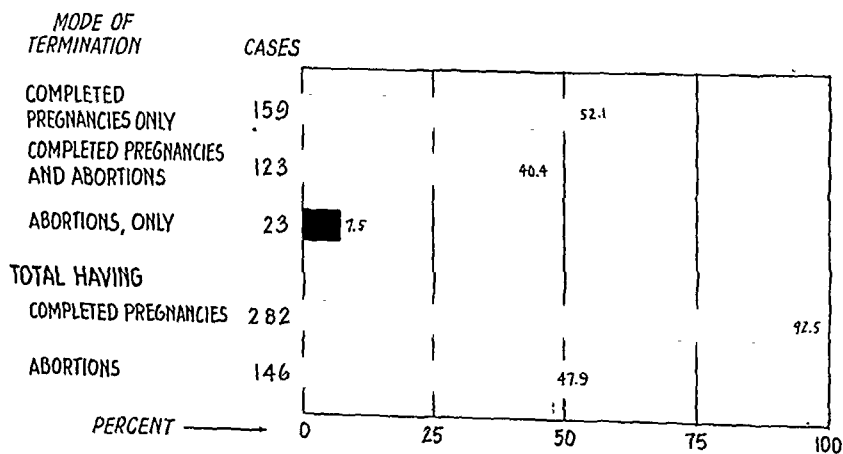


Fig. 3.

## INTERVAL SINCE LAST PREGNANCY

A prevalent idea concerning ectopic pregnancy is that this condition is usually preceded by a long period of sterility. It is to be noted that approximately 25 per cent had their last pregnancies within two years, 44 per cent within three years, 61 per cent within five years.



Of 49 women whose first pregnancy was ectopic, 11 were unmarried and may be presumed to have used contraceptive measures. Of the remaining 29 cases whose length of married life could be learned, 41

## WOMEN WITH ECTOPIC PREGNANCIES WHOSE LAST PREGNANCY OCCURRED WITHIN SPECIFIED TIME

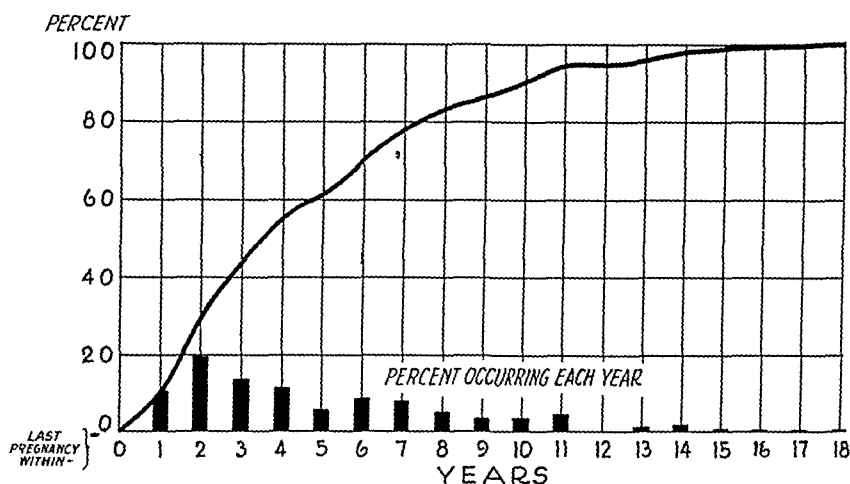


Fig. 4.

## WOMEN WITH ECTOPIC FIRST PREGNANCIES WHO WERE MARRIED WITHIN SPECIFIED TIME

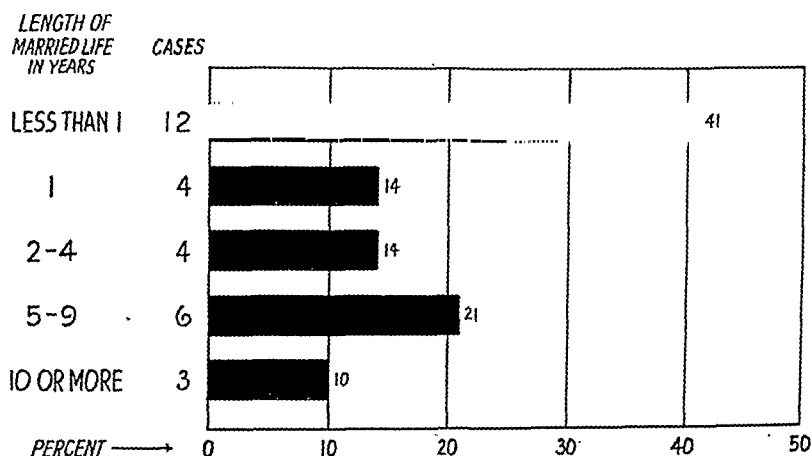


Fig. 5.

per cent became pregnant within one year, and 55 per cent in less than two years. Among the others of longer duration, a certain percentage no doubt practiced contraception. If the fault is presumed to be in the male in about 50 per cent of the cases, it is apparent we have

remaining only a small number who could be called relatively sterile. (Figs. 3, 4, 5.)

## PAIN

Abdominal pain was present in some form in every case where the history was reliable or complete. This pain is characteristically variable, with sudden exacerbations, and perhaps days or weeks of ab-

## CHARACTER OF ABDOMINAL PAIN IN ECTOPIC PREGNANCIES

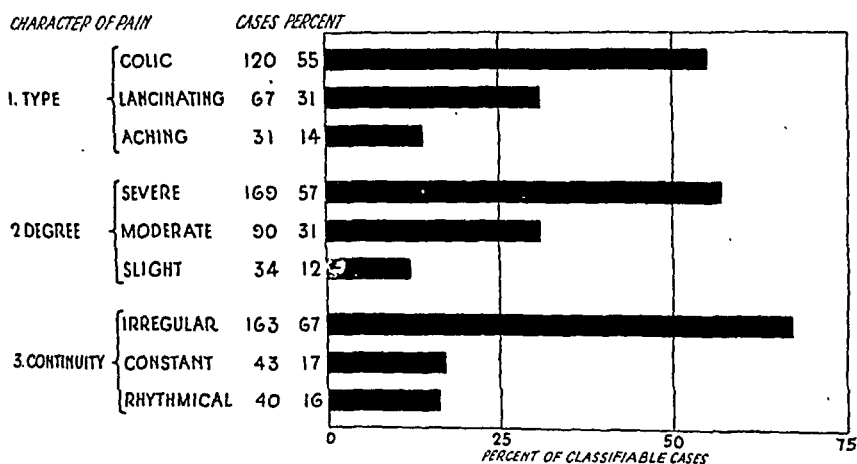


Fig. 6.

TABLE I. RADIATION OF PAIN IN ECTOPIC PREGNANCIES

PART AFFECTED	NUMBER OF CASES	CASES WITH OTHER PARTS SIMULTANEOUSLY AFFECTED
Arm	1	1
Shoulders	37	17
Right	20	11
Left	2	2
Both	13	3
Not stated	2	1
Back	38	12
General	34	11
Lumbar region	4	1
Chest	10	5
Abdomen	26	4
Umbilicus	1	1
Epigastrium	18	3
General	7	
Pelvic region	29	7
Hip	2	
Rectum	19	6
Perineum	3	3
Vagina	6	2
Legs	15	8
Right	3	
Left	3	
Both	9	8

sence. Any attempt to classify it is difficult, because nearly all the types may be found in the same patient. Fig. 6, therefore, is a comparison of the predominant type in each case as brought out by a study of the whole history. It was not found that pain had any particular relationship with vaginal bleeding, although one was frequently closely followed by the other. The radiation of pain, especially to the chest or shoulders is important in diagnosis, as it probably signifies free intraperitoneal bleeding. The apparently much more common radiation to the right shoulder might be explained by attempts of the examiner to elicit symptoms of appendicitis or gall bladder disease. (Table I.)

### TIME ELAPSED FROM LAST MENSTRUAL PERIOD TO APPEARANCE OF FIRST SYMPTOMS OF ECTOPIC PREGNANCY

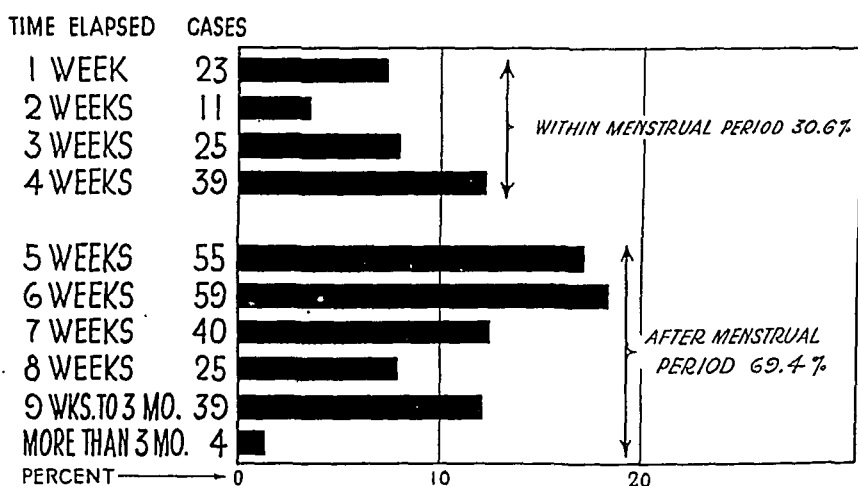


Fig. 7.

### VAGINAL BLEEDING

This resembles the abdominal pain in that it is extremely irregular and subject to remissions. The description was often indefinite, and classification is necessarily limited to outstanding features. A large majority had only slight or spotty bleeding, and long intervals with none at all. Often the only bleeding was an abortive type of menstruation at or near the regular time. A careful and detailed inquiry into the alleged last regular menstruation will frequently reveal this anomaly. There were nineteen who reported no vaginal bleeding and fourteen of these had gone beyond their regular menstrual time. Decidual casts were seldom reported by the patient or identified in the hospital. (Fig. 7.)

## GENERAL SYMPTOMS

These are due to acute anemia and peritoneal or visceral irritation. An extremely valuable, but a frequently missed symptom, is the sudden asthenia due to shock from even slight internal hemorrhage. This is only a minor degree of fainting and is manifested by vertigo, sudden amblyopia, or "dark spots" before the eyes, "cold sweat," or such muscular weakness that the patient is forced to sit or lie down. This symptom, being transient and overshadowed by the accompanying pain, will often be undiscovered unless specifically inquired for in the history. Alone or with actual fainting it occurred in 57 per cent of the histories and even this figure is probably to be taken as minimal.

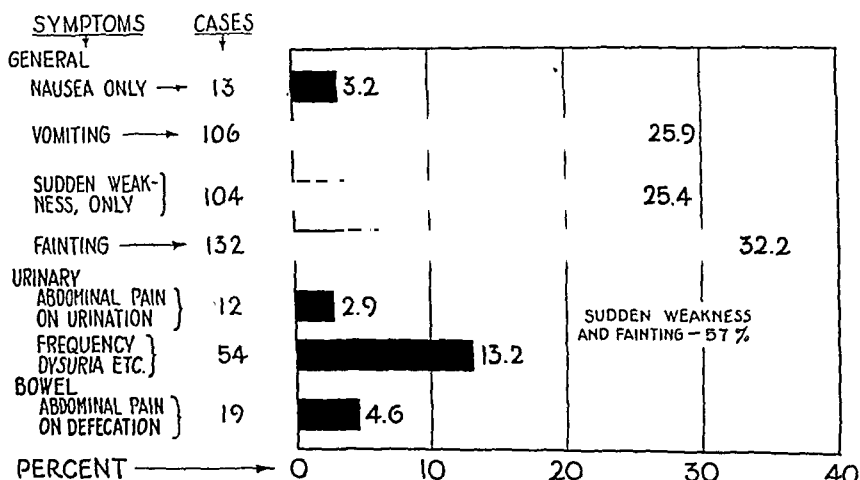
SYMPTOMS  
IN ECTOPIC PREGNANCIES

Fig. 8.

Nausea and vomiting were frequent (25.9 per cent) and may confuse the diagnosis with appendicitis. Morning sickness and breast changes were very seldom reported. Urinary symptoms were frequent but not characteristic. Abdominal pain on urination or defecation is suggestive but not typical or frequent. (Fig. 8.)

## ABDOMINAL EXAMINATION

This yields nothing that is not common to other conditions. The tenderness is usually somewhat less than that of pelvic inflammation or appendicitis. The mass found is often revealed to be the uterus displaced forward by the hematocele. Cullen's sign was rarely seen and occurred twice in the same patient who had two ectopics. Distention, together with nausea and vomiting were common in this series,

and may lead to a diagnosis of peritonitis or intestinal obstruction. In most cases, however, they are probably signs of peritoneal irritation. In 36 cases the abdominal examination was described as negative.

#### VAGINAL EXAMINATION

So much difficulty was experienced in tabulating the vaginal findings that a brief description is substituted.

The cervix was often reported softened and in a few cases to have a bluish discoloration. As both of these are present in many other conditions, including premenstrual congestion, it is our opinion that they are not particularly important in ectopic. Nor was the cervix in the majority of cases reported unusually tender on motion. When, how-

### WHITE BLOOD COUNT AND PERCENT OF POLYNUCLEAR LEUKOCYTES IN ECTOPIC PREGNANCIES

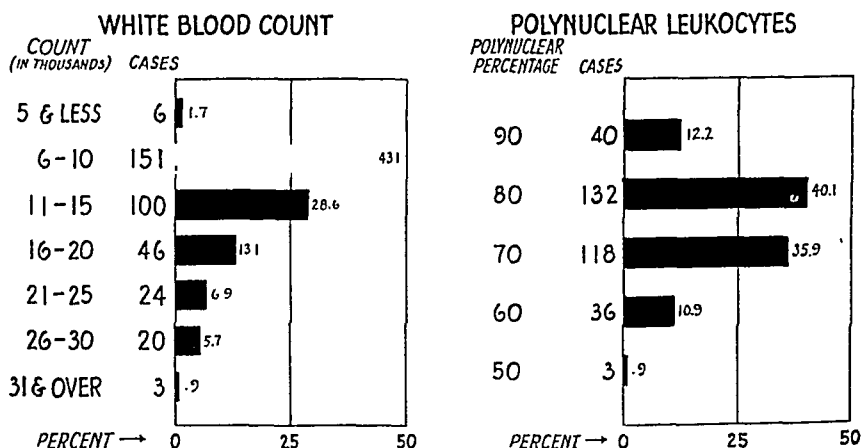


Fig. 9.

ever, acute pelvic inflammation can be ruled out, this sign may be considered highly suggestive of ectopic.

The uterus was usually found forward and was frequently described as being slightly enlarged and soft. The fundus was in many cases confused with the ectopic mass and is apt to be displaced in any direction from its normal position. A frequent early diagnosis was retroversion with threatened abortion, the small fundus being obscured by the larger soft mass behind it.

In about 10 per cent no mass was palpable. The masses in an overwhelming majority were described as soft, boggy, doughy, indefinite in outline, slightly movable, and in most cases surprisingly free from marked tenderness. In only a small number was the mass described as pulsating. Often another mass was found on the opposite side, and

in more than half the cases a mass was felt in the culdesac. Recto-vaginal examination was found best for the detection of free blood in this location.

## RED BLOOD COUNT IN ECTOPIC PREGNANCIES (AVERAGE DURING PERIOD OF OBSERVATION BEFORE OPERATION)

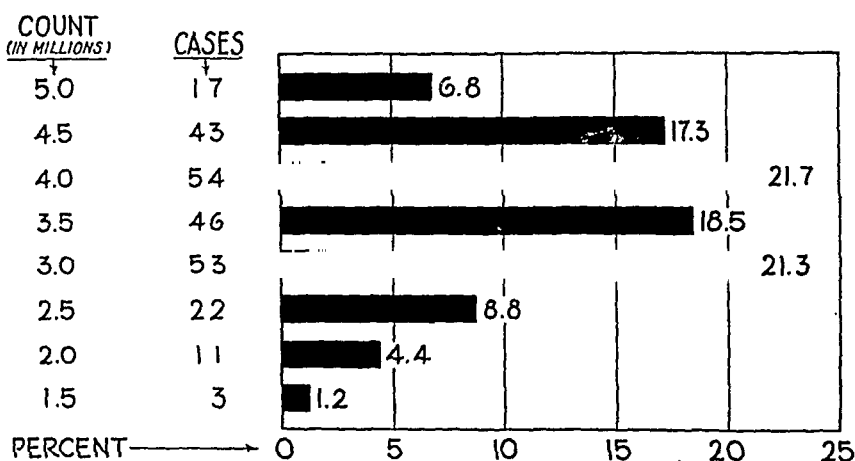


Fig. 10.

## HEMOGLOBIN IN ECTOPIC PREGNANCIES (AVERAGE DURING PERIOD OF OBSERVATION BEFORE OPERATION)

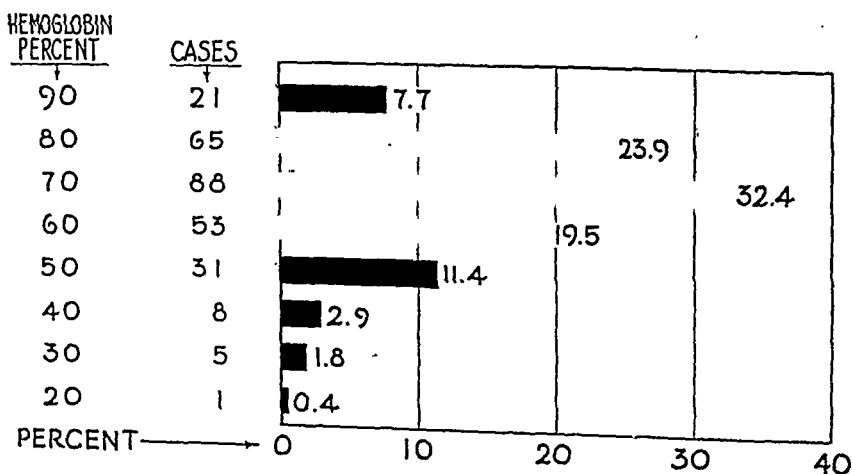


Fig. 11.

### CLINICAL FINDINGS

Temperature in the great majority was normal. When elevated there is probably an infection of the blood mass, more common in old neglected

cases. Occasionally a fresh severe hemorrhage is accompanied by a temporary rise, but this quickly reverts to normal.

Pulse readings and blood pressure were found to be normal in the largest number. Frequent readings are of course valuable to determine active hemorrhage and operative prognosis. Toxic and cardiorenal complications may confuse the diagnosis.

White blood count was normal in the majority of cases. Another large group, ranging from ten to fifteen thousand, usually had a normal temperature and long sedimentation time and might be accounted for by absorption of extravasated blood. When the count was higher it indicated either active or severe recent hemorrhage or virulent infection. In this group the sedimentation test is invaluable.

### SEDIMENTATION TEST OF CASES OF ECTOPIC PREGNANCIES COMPARED WITH OTHER CONDITIONS

PERCENT OF TESTS COMPLETED WITHIN SPECIFIED TIME

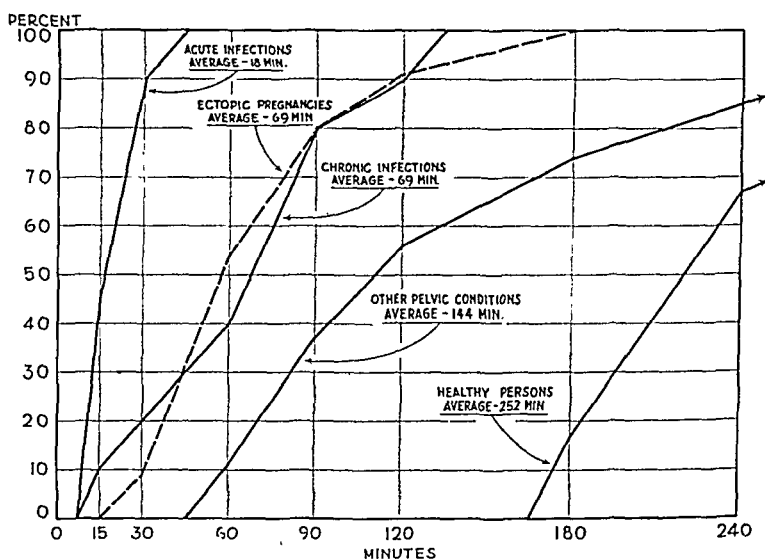


Fig. 12.

Red blood count and hemoglobin showed a slight average reduction. Obviously the amount of recent vaginal bleeding must be taken into consideration. Frequently repeated readings, preferably by the same examiner, are important in the detection of active bleeding. Type of blood was No. 1 in 44 cases, No. 2 in 34, No. 3 in 8, and No. 4 in 2. Wassermann was 2+ or more in 12 of the last hundred cases. (Figs. 9, 10, 11.)

#### SEDIMENTATION TEST

Our series is unfortunately small, as we have adopted this test only during the last eighteen months. The chart shows the result in 120 cases of various conditions for comparison. It is to be noted that the time in ectopic pregnancy followed a fairly wide range, but closely

paralleled that found in chronic infections, and had a decided variation from acute infections and noninfected conditions. When the time was short in ectopic, it almost infallibly pointed either to an infection of the hematocele or to a coincident infection elsewhere. The chart would seem to indicate that in a majority of cases the free blood and clots or even the products of conception may either contain some latent infection or act on the blood plasma in a fashion similar to infection. However, when the sedimentation time was rapid, the abdominal blood had usually been present for a number of weeks. This test is of great value and reliability in the determination of infection. We consider it superior to the leucocyte count. Its interpretation in the diagnosis of ectopic must be taken only in conjunction with other clinical facts. (Fig. 12.)

#### OPERATIVE FINDINGS

The right and left tubes were about equally involved, 131 on the right and 124 on the left. As tubal abortions usually have their origin in the outer portion of the tube, adding these to the tubal ruptures it was found that the predisposition to ectopic implantation progressively increased from the uterus toward the outer extremity.

There were twelve interstitials, one ovarian, and one abdominal pregnancy. Twin fetuses were observed three times, but there was no case of authentic bilateral tubal, or coincident uterine, pregnancy.

In this series rupture was over three times as common as abortion. Many of the so-called unruptured cases showed some evidence of beginning rupture or abortion with free intraperitoneal blood. From the very small number of truly unruptured cases seen, it is our impression that the symptoms and signs must be so slight and misleading as to make the diagnosis largely a matter of chance, and consequently replete with error.

The opposite tube was described as normal in 103, showing chronic inflammation in 81, hematosalpinx in 8, and was absent in 22 cases. In addition, the spreading hematocele with omentum and adhesions was frequently extensive enough to give the preoperative impression of bilateral mass.

#### SUMMARY OF TWELVE INTERSTITIAL PREGNANCIES

There were symptoms of shock in seven cases with corresponding rapid pulse, low blood pressure, and signs of severe anemia. Four had never been previously pregnant. Five out of nine gave no history of vaginal bleeding. In five the major symptoms occurred within four weeks of the last regular menstruation and none were over six weeks from this last period. There were two deaths; one occurring a few minutes after the patient arrived in the hospital, and one postoperative death, an operative mortality of 9 per cent.



## ADDITIONAL AIDS TO DIAGNOSIS

Vaginal examination under anesthesia we consider to be hazardous and misleading, and rarely necessary.

Colpotomy is extremely valuable where there is an easily accessible mass in the culdesac which cannot be differentiated from a collection of pus. The disadvantages of this procedure are the possibility of introducing infection or increasing internal hemorrhage, and undesirable addition to operative trauma. In this series colpotomy was done 33 times and in 3 instances a postoperative pelvic infection appeared to have been the result. It is our opinion that the colpotomy wound should be closed without drainage in these cases.

## ACCURACY OF DIAGNOSIS IN ECTOPIC PREGNANCIES

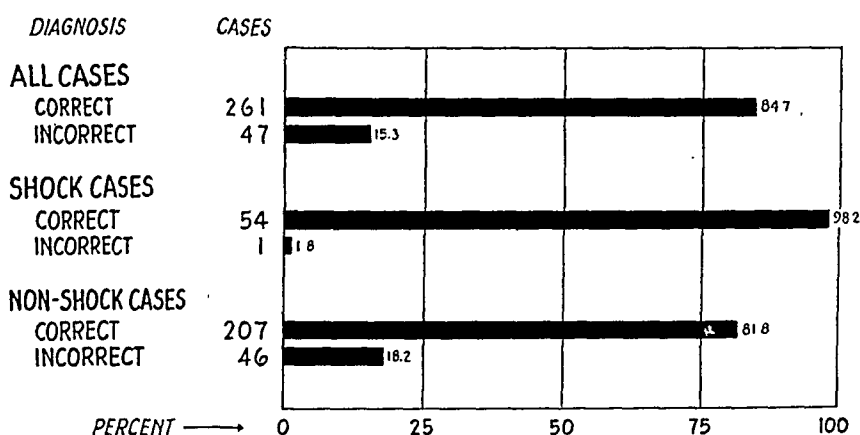


Fig. 13.

Aspiration of the vaginal vault is valuable under the same conditions, but is also not without danger.

Exploratory laparotomy is always an acknowledgment of diagnostic defeat. Frequently, however, the symptoms may be so alarming or the pathology so obviously requiring surgical interference that prompt operation even without a positive diagnosis is clearly indicated.

## ACCURACY OF DIAGNOSIS

The diagnosis of ectopic pregnancy can most readily be made at or shortly after the occurrence of any degree of internal hemorrhage. Early in the condition the signs and symptoms may be extremely slight or indefinite, examination may show very little, and at this time there is a close resemblance to normal pregnancy with threatened abortion. Later the blood becomes clotted, organized or encapsulated, with adhe-

sions, possibly infected, and giving symptoms of pressure and mild toxemia from reabsorption. The appearance then is apt to simulate pelvic inflammation. (Fig. 13.)

Threatened or incomplete abortion and acute salpingitis are not usually revealed as preoperative diagnoses, because as such they would not come to laparotomy. Nevertheless, they are very frequently the first diagnosis. Appendicitis and other conditions not involving the pelvic organs do not appear in Table II, because these cases are transferred to the General Surgical Division of the hospital.

Previous to 1918 there were many unlabeled cases and in fact diagnosis was too often made by colpotomy or exploration. These were excluded from the table. Dr. F. C. Holden at that time instituted the rule that a written and preferably single preoperative diagnosis must be recorded by the operating surgeon.

TABLE II. DIAGNOSIS MADE IN FORTY-SEVEN WRONGLY DIAGNOSED ECTOPIC PREGNANCIES

DIAGNOSIS	NUMBER OF CASES	PERCENTAGE OF TOTAL CASES
Total cases	47	100
Adnexal disease, only	26	56
Ovarian cyst	7*	15
Abortion	4*	9
Fibromyoma	2	4
Pelvic abscess	2*	4
Ruptured uterus	1	2
Acute appendicitis	1	2
Retroverted uterus with adnexal disease	1	2
Retroverted pregnant uterus	1	2
Peritonitis	1	2
Uterine polyp	1	2

\*One case with adnexal disease also.

Our total percentage of error was 15.3. The only mistake among the shock cases was a fairly advanced abdominal pregnancy which was thought to be a ruptured uterus. The figures take into account only ectopics which were wrongly diagnosed. If the cases diagnosed as ectopics which proved to be something else were taken into consideration, the total error would be very much higher.

#### COMMENT

From the foregoing it will be seen that the diagnosis of ectopic pregnancy is still difficult and puzzling in a very large number of cases. Unfortunately, we can expect very little except negative help from the laboratory. A correct diagnosis depends on complete and accurate history combined with proper interpretation of all clinical data. Perhaps most ectopics are overlooked during their early stage because the attendant had his mind fixed on the more common conditions and did not think of the possibility of ectopic. At times,

too, the first impression is ectopic, but owing to the confusion of symptoms, or fixing the attention on one phase, or overcaution engendered by a few mistakes in the past, the diagnosis is incorrectly made.

#### CONCLUSIONS

1. In a majority of cases a preceding period of unusual infertility was not demonstrated.

2. A previous history of severe inflammatory pelvic disease was seldom reported.

3. History of previous pregnancies closely approximates that of the married population of this age group.

4. A large incidence of previous operations on the uterus and adnexae was revealed.

5. Predominant type of abdominal pain is irregular, lancinating or colicky, and subject to remissions.

6. Vaginal bleeding is most frequently irregular and scanty.

7. Actual fainting or its minor manifestation of sudden weakness was present in at least 57 per cent of the cases. This symptom is almost pathognomonic and, in relation to type of abdominal pain and vaginal bleeding, will establish a diagnosis in the largest number of cases.

8. Except in the presence of infection or recent hemorrhage, temperature, pulse, blood pressure, blood count, and sedimentation time are approximately normal.

9. A closer scrutiny of the alleged last menstruation will often reveal an anomaly which may clarify the diagnosis.

10. More reliance may be placed on the history than on physical examination.

515 PARK AVENUE.

(For discussion, see page 439.)

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**Pastiels: Dystocia Due to an Ovarian Cyst. Suprapubic Cesarean Section Followed by Oophorectomy. Bruxelles-med. 8: 175, 1927.**

Pastiels reports in full a case of mucoid cyst of the left ovary discovered during the sixth month of pregnancy. The patient was kept under close observation. After two hours of labor the head had not engaged and the cyst was presenting in the pelvis. A low cesarean section followed by left oophorectomy was therefore done. The child was normal and the mother made an uneventful recovery.

In 278 cases reported in literature where the cyst was within the pelvis, Puech and Vauvert ascertained dystocia in 262. These authors also feel that the earlier in pregnancy the cyst is removed the less is the chance of spontaneous abortion. Pastiels, therefore, advocates operative removal before the third month. After this time he intervenes only in case of emergency, letting the patient go to term and doing a cesarean section and oophorectomy at that time if circumstances warrant this procedure.

THEODORE W. ADAMS.

# MATERNAL MORTALITY IN 582 ABDOMINAL CESAREAN SECTIONS\*

(From the New York Nursery and Child's Hospital)

By E. M. HAWKS, M.D., NEW YORK CITY

THE maternal mortality of cesarean section has been much discussed in the last few years. It is high and the reasons are being sought. The problem is not alone that the rate is high but rather that there are too many deaths due to cesarean section. Analyses of complete groups of cases are, therefore, in order, and this report is a review of the deaths following the abdominal cesarean sections done at The New York Nursery and Child's Hospital during the years from 1910 to 1928, inclusive. This period covers the work of the hospital as it is now organized. The private cases are included and acknowledgment of this privilege is hereby made.

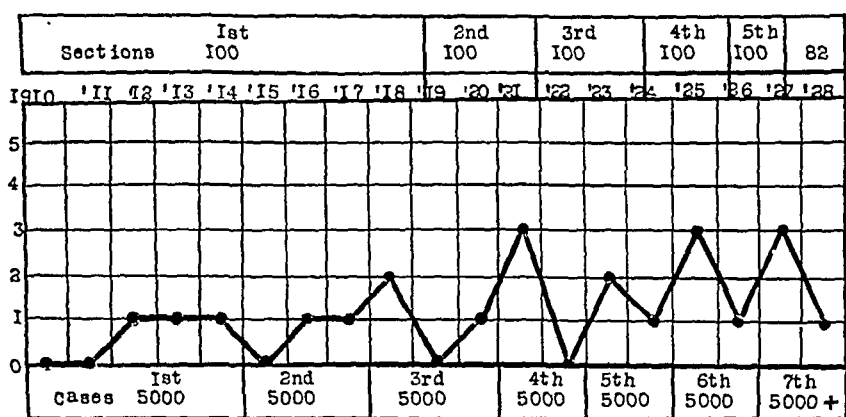


Fig. 1.—Number of deaths yearly.

This series is of particular interest because the operations have been done by so many men. Nearly all the obstetric groups in New York City are represented. There were 83 operators and 37 of them have been, or are, members of this Society.

The following topics will be considered:

First: The number of deaths, the rate, and the part of the total mortality formed by these deaths.

Second: The incidence and its bearing on the mortality.

Third: The causes of death.

Fourth: Variety and choice of type of operation.

There were 22 deaths, distributed according to years as shown in Fig. 1. An increase is noted. There were 7 deaths in the first half of the time and 15 in the second. This picture is probably typical of what

\*Read at a meeting of the New York Obstetrical Society, March 12, 1929.

is happening in many hospitals throughout the country. The number of cesarean sections has been greater and there have been more cases as the years have passed, but the deaths have increased in number slightly faster than have the cases.

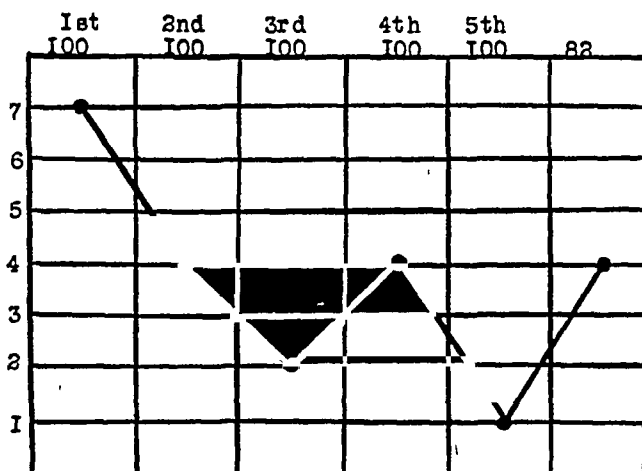


Fig. 2.—Death rate of cesarean section per groups of 100 cases.

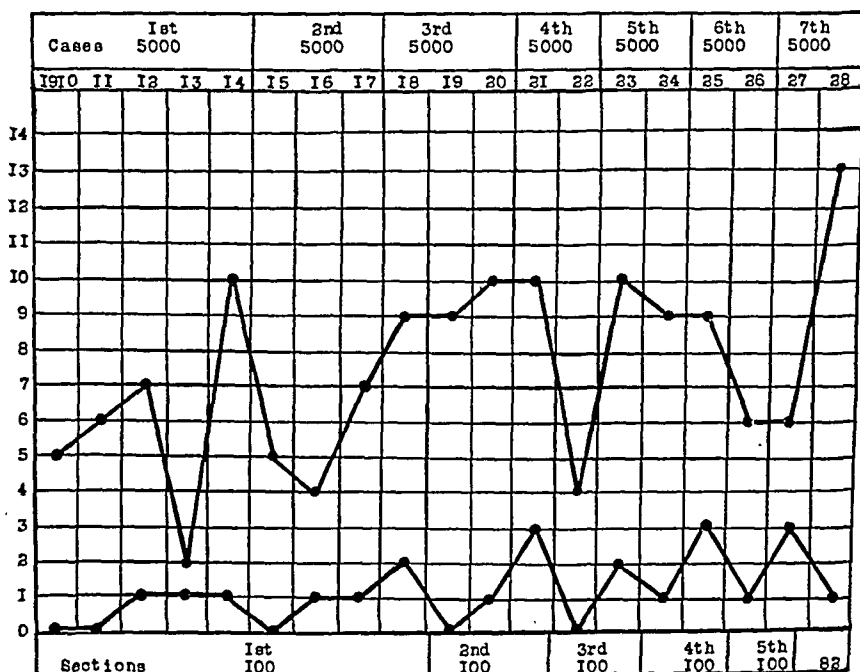


Fig. 3.—Total mortality and that from cesarean section by years.

The total death rate was 3.6 per cent, as shown in Fig. 2 in groups of 100 cesarean sections.

Figs. 3, 4, and 5 show the part of the total mortality formed by deaths following section. Fig. 3 shows both mortalities according to years. There was a total maternal mortality, uncorrected, of 141 in

35,677 cases. This is a percentage of 0.4 or 40 per 10,000. Section was a factor in 6+ deaths. Fig. 4 shows more clearly the trends of these mortalities as the cases are arranged in large groups of 5000. Deaths

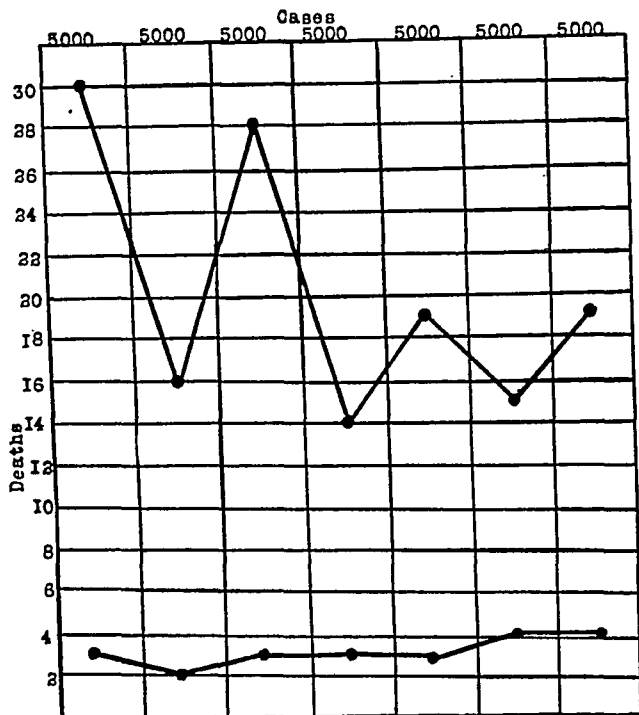


Fig. 4.—Total mortality following cesarean section.

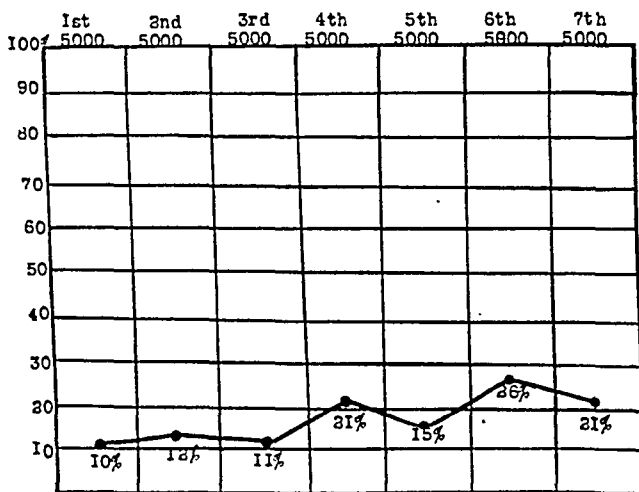


Fig. 5.—Shows the percentage that the deaths from cesarean section formed of the total mortality.

from section are seen to form a larger part of the total mortality as the years pass. Fig. 5 shows, in percentages, the part of the total mortality, in groups of 5000 cases, formed by deaths after cesarean section. The percentage rose from 10 per cent to 26 per cent and in the last

group dropped to 21 per cent. The average was 16 per cent. It may be said that this percentage is high because the total mortality is low. If a patient died in the years 1910 to 1914 there was one chance in ten of her having died after cesarean section. In 1927 or 1928 there was one chance in five of cesarean section having been a factor in her death.

### INCIDENCE

Table I gives a complete statement of the incidence of cesarean section for the nineteen years. The number of cases, the cesarean sections with the percentage and rate of incidence, the deaths from cesarean section, and also the number of primary and repeated cesarean sections

TABLE I. SHOWING NUMBER OF CESAREAN SECTIONS IN EACH YEAR, AND DEATHS FOLLOWING CESAREAN SECTION FOR EACH YEAR

YEAR	CASES	TOTAL CESAREAN SECTIONS	PER CENT	RATE	DEATHS	REPEATED CESAREAN SECTIONS	PRIMARY CESAREAN SECTIONS
1910	913	3	0.3	1 in 300	0	0	3
1911	557	1	0.2	1 in 500	0	1	0
1912	1080	6	0.6	1 in 160	1	0	6
1913	1169	3	0.3	1 in 300	1	0	3
1914	1238	9	0.7	1 in 140	1	1	8
1915	1529	8	0.5	1 in 200	0	1	7
1916	1541	10	0.6	1 in 160	1	0	10
1917	1849	19	1.0	1 in 100	2	2	17
1918	2256	23	1.0	1 in 100	2	1	22
1919	2003	37	1.8	1 in 55	0	5	32
1920	2386	36	1.5	1 in 66	1	7	29
1921	2300	47	2.0	1 in 50	3	10	37
1922	2395	39	1.6	1 in 62	0	4	35
1923	3005	35	1.2	1 in 80	2	5	30
1924	2277	61	2.7	1 in 37	1	12	49
1925	2227	51	2.3	1 in 43	3	12	39
1926	2198	71	3.2	1 in 31	1	19	52
1927	2399	64	2.7	1 in 37	3	16	48
1928	2355	59	2.5	1 in 40	1	18	41
19 years	35677	582	1.6%	1 in 62	22 (3.6%)	114	468

for each year are given. The rate of incidence for the whole number of cases as 1 in 62, or 16 per thousand, or 1.6 per cent. The rate for the primary cesarean section was 1 in 80, or 13 per thousand, or 1.3 per cent.

The incidence is seen better graphically in Fig. 6. It is arranged so that the rate per thousand each year is given. There is a rapid rise from 3 and 2 per thousand in the beginning to 32 per thousand in 1926 and a fall in 1927 and 1928 to 25 per thousand.

Fig. 7 shows a smoother curve of the incidence as it is based on groups of 5000 cases. The broken line is the curve of the primary cesarean sections. The upper line is the curve of the total incidence. The space between the two lines represents the repeated cesarean sections. This space is seen to be steadily increasing. The rise in the curves is due, no doubt, to the surgical solution of the difficult cases.

The indications have been widened as the ease and safety of surgery have been realized. This picture, also, is probably common to most hospitals. The decrease in the incidence seems to be due to better hospital labor and to improved means of vaginal delivery. The obstetrician has felt a sense of security in the newer types of cesarean section. He has consequently allowed the cases to go to full dilatation and to have much better trial labors. He has been able to meet the situation of possible infection without fear if cesarean section has been necessary. Rectal analgesia has been very helpful in getting full dilatation without loss of the patient's morale. Confidence has been had, also, in the use of mercurochrome during labor. The Barton and the Kiel-

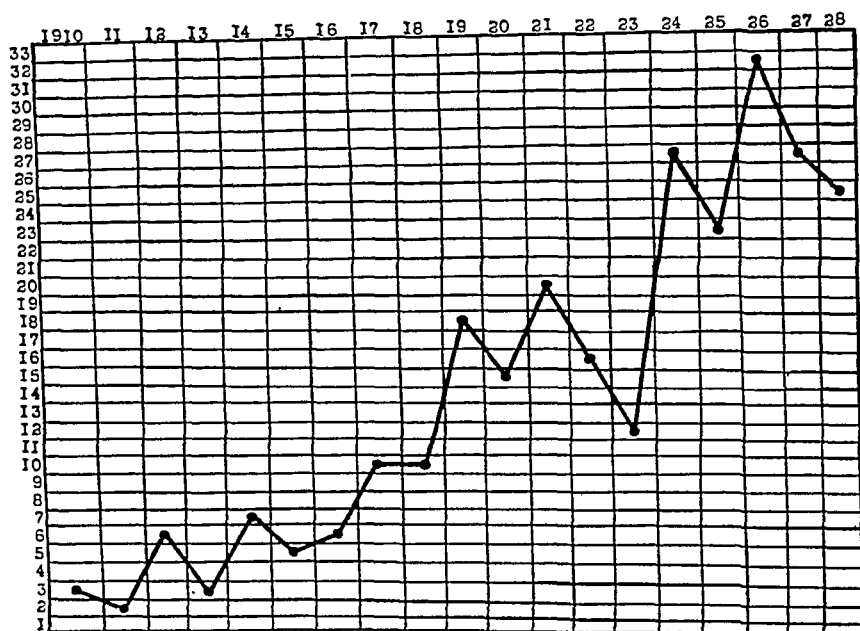


Fig. 6.—Incidence of cesarean section. Rate per year per 1000 cases.

land forceps, as well as better technic in version and extraction, due to Potter's teaching, have improved means of vaginal delivery. They have helped in the deliveries of women who might have been sectioned.

A further analysis of the incidence is seen in Fig. 8. The private and public cases for the past eight years are separated and the incidence per thousand cases in each year is shown for both groups. There were 285 cesarean sections in 7515 private patients. This is an incidence of 3.8 per cent. There were 141 cesarean sections in 11,640 ward patients. This is an incidence of 1.2 per cent. There were ten deaths in the private and four in the ward patients.

The lower curve is probably close to that of the essential incidence for mother and baby. In cases of contracted pelvis or of disproportion, the mothers as a rule had sufficient labor to prove almost positively the



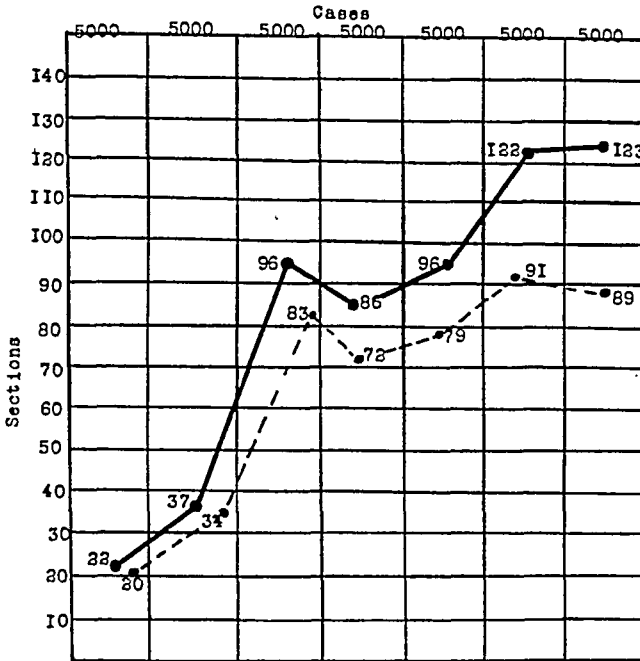


Fig. 7.—Incidence of cesarean section per groups of 5000 cases.

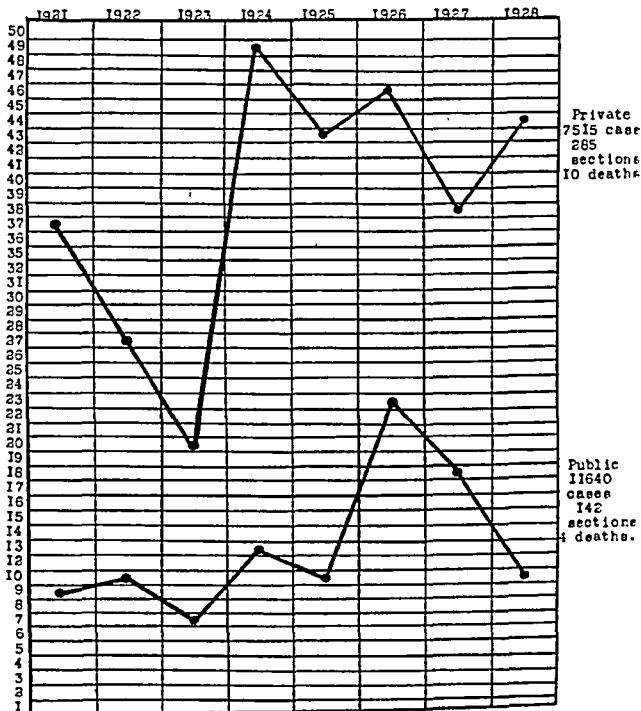


Fig. 8.—Incidence of cesarean section in private and public cases. The rate per 1000 cases per year is shown.

necessity of cesarean section. Other indications had the scrutiny and discussion of the ward service. There were no craniotomies on normal living babies.

The chief reason for the higher course of the upper curve has been the arbitrary choice of cesarean section in the private case. It is doubtful whether there has been a higher percentage of abnormal cases in the private service. Some capable obstetricians have deliberately chosen section in preference to the vaginal delivery in their debatable cases. The anxiety about the private case has played a part in this choice. Other men who have had more experience in abdominal surgery than in obstetrics have also followed the line of least resistance

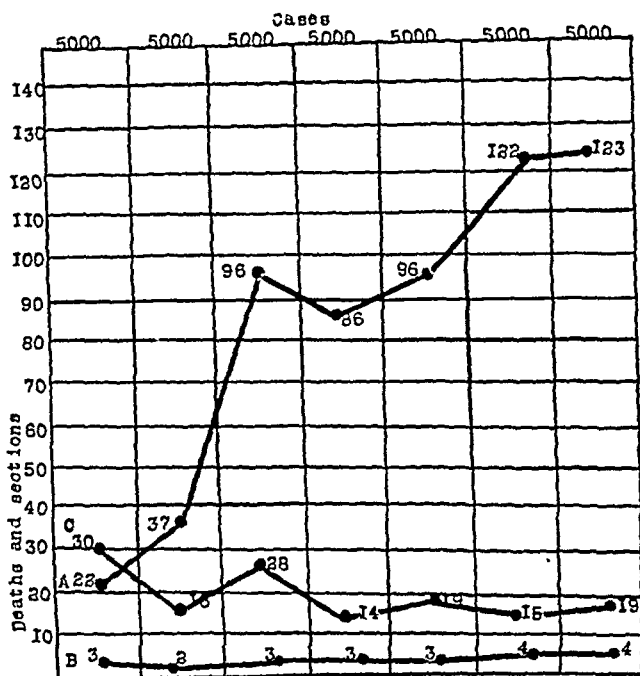


Fig. 3.—Relationship between incidence (A) and the mortality following cesarean section (B), and the total mortality (C).

and have done cesarean sections on many of their patients. Consultations do not always safeguard as they are often merely politely agreeable. This curve, then, may indicate an arbitrary incidence as opposed to an essential one.

This arbitrary or high incidence may be the result of the judgment of good obstetricians or of the demand of the parents for the safety of their babies, but it is one of the causes of the rising maternal mortality about which we are concerned. When cesarean section is chosen the consequences should be remembered. The first result is more deaths from one cause or another. We have seen in this last chart that there were 10 deaths from cesarean section in 7515 private patients and 4 in 11,640 ward patients. Then there is the aftermath of danger of rupture of the uterus in the succeeding pregnancy, danger from the in-

creased rate of mortality of the repeated section, and also the dangers associated with ventral hernia, adhesions, and with therapeutic abortion. Finally there is the end-result of disturbed marital relation and limited productivity.

The relationship between incidence and mortality in this series of cases is seen in Fig. 9. The mortality following cesarean section has not, as a matter of fact, been affected very much by the rapid rise in the incidence. It has been increased by only one in each of the last two groups of 5000 patients or two in 10,000. The complications and sequelae have not been estimated. It seems even fair to ascribe some of the lowering of the total mortality to the increase in the incidence of cesarean section. Other factors, of course, have been prenatal care, improvement in prevention, and in the treatment of infection, and transfusion. In the first 5000 cases there were 22 cesarean sections and 30 deaths from all causes, while in the last 5000 cases there were 123 sections and 19 deaths from all causes. Among the indications for the 123 cesarean sections there were 66 in the interest of the mothers, including 34 repeated cesarean sections. The best results were in the fourth group of 5000 in which there were 86 cesarean sections with a total of 14 deaths from all causes including the 3 deaths from the cesarean sections.

#### CAUSES OF DEATHS

The causes of the deaths, arranged chronologically, following cesarean section are shown in Table II. It seems safe to say that a lowering of the mortality following section may be expected in the future. Deaths from cesarean section in eclampsia are becoming rare. The last in this series was seven years ago. This indication is being eliminated by better prenatal care and by a change in the method of treatment. The deaths from shock, and from hemorrhage and shock, may occur again but with better general or local anesthesia and with the modern use of transfusion, they will be few. Pneumonia, too, should be less frequent. Improved anesthesia and present day precautions will cut down its incidence. We were fortunate in not having more deaths in bad cardiac cases. These cases are being studied more carefully now in a special cardiac clinic.

Paralytic ileus has been common to a greater or less degree in the classical cesarean sections but this type of operation is being limited more and more to the clean cases, and we may expect less ileus. It is seen less often anyway on account of better pre- and postoperative care. The case of antepartum intestinal obstruction was a rarity and was well advanced on admission. The patient was at term and cesarean section was done. Surgical treatment of the obstruction failed.

The two cases of tuberculous meningitis, associated with spinal anesthesia, were startling. The death from postoperative hemorrhage shows

the danger of additional work in cases of cesarean section. Autopsy showed that the bleeding came from an injury to a large vein in the broad ligament following salpingo-oophorectomy. The death after transfusion was very puzzling. The cesarean section was done for placenta previa. On the fifth day a transfusion was given. The patient was doing well but the red cell count was low. There was no unfavorable reaction. On the seventh day another transfusion was given as an additional boost. The patient had a chill, became cyanotic, and died in coma three hours later. There were no untoward symptoms during the transfusion. The blood was retyped before the transfusion and postmortem. There were 4 deaths in the group of repeated cesarean sections. In the last 6 deaths cesarean section may be exonerated from directly causing the fatalities. There was only one death from septicemia. Possibly there may be more such deaths in a second group of cases as large as this one. There were 7 deaths from peritonitis in the contaminated cases. It should be noted that the last such death oc-

TABLE II

INDICATION			CAUSES OF DEATH
1	1912	?	Shock
2	1912	Eclampsia	Died after 7 hours. Eclampsia
3	1914	Cervical dystocia. Bagged twice. Labor three days	Peritonitis, 3 days
4	1916	Eclampsia	Shock, 7 hours
5	1917	Contracted pelvis	Peritonitis, 4 days
6	1918	Contracted pelvis, bagged	Septicemia, 10 days
7	1918	Dystocia due to amputation of cervix. Labor 60 hours	Peritonitis, 3 days
8	1920	Preeclamptic toxemia	Pneumonia
9	1921	Cardiac, decompensated	Died after 22 hours
10	1921	Eclampsia	Eclampsia, 20 hours
11	1921	Rigid cervix	Peritonitis, 3 days
12	1923	Preeclamptic toxemia	Paralytic ileus, 4 days
13	1923	Contracted pelvis, previous section	Hemorrhage, shock, 3 hours
14	1924	Rigid cervix, labor 30 hours	Peritonitis, 4 days
15	1925	Premature rupture of membranes, contracted pelvis, labor 24 hrs.	Peritonitis, 4 days
16	1925	Induction of labor, bagged twice, membranes ruptured artificially, weak pains 48 hours. Temp. 103.4°	Peritonitis, 4 days
17	1925	Intestinal obstruction, antepartum	Intestinal obstruction
18	1926	Previous cesarean section	Pneumonia
19	1927	Contracted pelvis, cervical dystocia	Tuberculous meningitis, spinal anesthesia
20	1927	Contracted pelvis, previous section	Tuberculous meningitis, spinal anesthesia
21	1927	Previous section, salpingo-oophorectomy	Postoperative hemorrhage
22	1928	Placenta previa	Died on 7th day, in coma 2 hours after second transfusion. Cerebral embolism or anaphylactic death

curred in 1925, or three years ago. The newer types of cesarean section will cut these deaths down in the future as has already been the case.

These contaminated cases with disproportion or cervical dystocia have formed a dangerous and difficult group. They have been the predisposing cause for almost one-third of the deaths. The choice has had to be made between almost hopeless deliveries or craniotomies with their consequences and cesarean sections with the danger of peritonitis. This decision has not been an easy one to make.

These cases have sounded the death knell of the classical cesarean section in the contaminated patient. It is true that the classical operation has been successful in many of them but the death rate has been high. An experienced and skillful operator may have good results. Each man knows his own work and knows how he can best handle a given problem. He should, however, be alive to improvement. In the classical operation an operator may succeed in protecting the peritoneal cavity from the initial spill but there is still danger from the secondary leakage or extension of infection from the uterus and, as a rule, no provision for its control. Some men have drained the peritoneal cavity to advantage in these cases.

#### VARIETY OF SECTIONS

Operations have been devised to avoid the dangers of initial spill and secondary leakage. Some have been abandoned as others more practical have appeared. Table III shows the variety of sections that have been used in this series of cases. It also gives the years in which the different kinds have been in use. From 1910 to 1922 there were only the classical and the Porro. The low flap operation was introduced in 1922.

TABLE III. VARIETY OF SECTIONS

	<i>Classical.</i> The Intraperitoneal Method. Sanger's Operation. High, mid, and low types.
	<i>Porro.</i> Hysterectomy.
1922	<i>Low Flap or Two Flap.</i> A cervical cesarean section Kronig's Operation. Modified by Beck. Laparotrachelotomy of DeLee.
1923	<i>Extraperitoneal Method.</i> Latzko's Operation.
1924	<i>Transperitoneal Method.</i> Fromme-Veit Operation. Hirst Operation. Modified by Brodhead, Langrock, and Cassasa and known as the <i>peritoneal exclusion</i> .

Table IV shows the number of cesarean sections done according to each type of operation and the number of deaths after each kind. It is seen that most of the cesarean sections have been classical and that all but one death have occurred in this variety. It will also be seen that 79 cases, mostly contaminated, have been done according to the newer types of operation and that no death has occurred.

TABLE IV. CESAREAN SECTIONS AND DEATHS ACCORDING TO TYPE OF OPERATION

	NO.	DEATHS
Classical	492	21
Porro	11	1
Low Flap	30	0
Latzko	30	0
Peritoneal exclusion	19	0

## CHOICE OF TYPE OF OPERATION

We have been fortunate at the New York Nursery and Child's Hospital in having been able to observe the methods of many operators. We have not adopted any one operation exclusively, believing that each has its place. We feel that at present the obstetric surgeon is able to choose a type of operation to fit his case. There are 5 forms of cesarean section from which he may pick. As in any surgical problem variations in conditions determine selection of type of operative procedure when several methods are available. So it would seem to be with cesarean section, for there is not much doubt that the operation suitable for a clean case is not the choice for a contaminated one. During the past few years other forms of cesarean section than the classical have been used in most of the contaminated cases. Some of the men have done the low flap exclusively, others the peritoneal exclusion, a few the Latzko, and others have done all forms as they have seen fit. This last viewpoint I wish to emphasize.

There has not been a death from peritonitis in the last 212 cesarean sections. All chances have been accepted as no craniotomies on normal living babies have been done. This is strong evidence of the value of the newer types of cesarean section in the contaminated cases. Some deaths from septicemia are bound to happen. The cesarean sections aim only at preventing peritonitis by controlling the initial spill and the later leakage from the uterine wound. They cannot prevent thrombophlebitis or infections from the uterus except inasmuch as they terminate labor. There may be anatomic hazards and technical difficulties involved but they are not to be compared with the risk of peritonitis.

There is no doubt that a combination of essential incidence, good choice of type of cesarean section, good operative technic and proper anesthesia will give the minimum mortality. If a man be inexperienced in the newer types of cesarean section it would be better for him to

operate early in labor. That means higher incidence with its consequences. Some men emphasize the importance of early operation but this should be second choice. There will always be contaminated cases and the obstetrician should fit himself to handle them properly.

In the selection of the type of cesarean section the classical operation is reserved for the elective case, i.e., the woman not in labor. It is useful when speed is essential, as in a case of accidental hemorrhage with little dilatation and mother and baby in danger. It may be easiest in a cardiac case or the choice in a clean case of placenta previa.

The other types are used in the potentially infected cases, although some of the operators have done the low flap operation in the clean and elective cases also. The choice is made usually according to the sup-

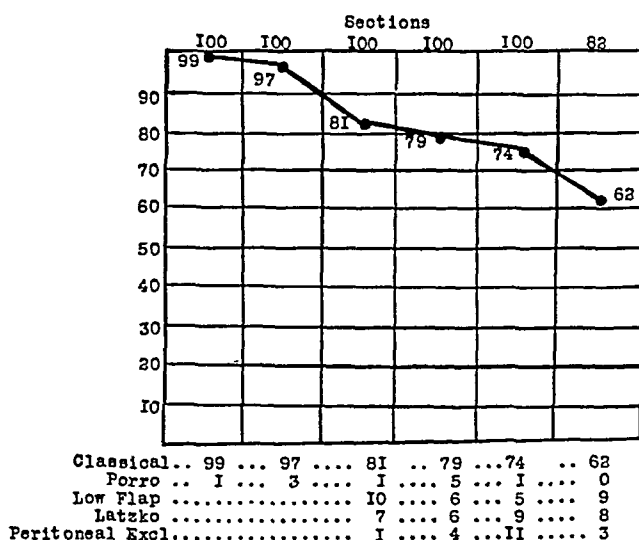


Fig. 10.—Declining curve of the classical operation.

posed degree of contamination in the order of first, low flap; second, peritoneal exclusion; third, Latzko; fourth, Porro.

Thus the low flap operation is done in a case in early or later labor with little or no contamination. Fourteen of the cases which had the low flap operation had had no labor. The average duration of labor in the remaining 16 was fifteen and one-half hours. The labor varied from three to forty hours. Four lasted twenty-four hours or longer. With local anesthesia and with the technic of Beck or DeLee this may prove to be the universal cesarean section.

The method of peritoneal exclusion is chosen in contaminated cases with suspected infection of the amniotic fluid. The initial spill or later leakage from the uterus is considered dangerous. The operation is particularly adapted to a case in which there is likely to be very little retraction of the lower uterine segment. This operation has the advantage of affording drainage if thought necessary. Four of the 19 pa-

tients on whom this operation was done had no labor. One of the 4 had ruptured membranes for three days. In the remaining 15, labor averaged twenty-six hours. The variation was from twelve to fifty-five hours. Eight were twenty-four hours or longer. Its simplicity recommends this operation. The technic described by Brodhead, Langrock, and Cassasa is the more preferred. So far it has given very good results in these rather badly contaminated cases.

The Latzko operation is the selection for the contaminated case long in labor and with the lower uterine segment well drawn up. There may have been much manipulation or possibly ineffectual attempts at delivery from below. This operation also has the advantage of drainage. The patients upon whom this operation was done had all been in labor. The variation was from eight to seventy-two hours. The average was twenty-nine hours. Nineteen had been in labor for twenty-four hours or longer. In the 30 operations of this type the bladder was injured four times. No fistulas resulted. The peritoneal cavity was opened 11 times. It was closed, however, before the uterus was incised.

There is no competition, in our opinion, between the low flap, peritoneal exclusion and Latzko operations, unless the low flap is used in the badly contaminated cases. In this group the peritoneal exclusion or Latzko is considered safer because of better protection of the peritoneal cavity and drainage. If the lower uterine segment is thought to be well retracted the Latzko operation is chosen, otherwise the peritoneal exclusion.

The Porro operation is the old choice for the badly contaminated case with a noncontractile, grossly infected uterus. It is also used in cases of uncontrollable hemorrhage, apoplectic uterus, nonremovable tumors, placenta accreta, and usually in cases of ruptured uterus. It was done only twice for infection in this series of cases.

#### SUMMARY

In 582 abdominal cesarean sections done in a single hospital by a large number of obstetricians during the past nineteen years, there were 22 deaths (3.6 per cent).

These deaths formed 16 per cent of the total obstetric mortality.

The average incidence was 1.6 per cent. In sixteen years it rose from 0.2 per cent to 3.2 per cent. In the last two years it has dropped to 2.5 per cent.

The mortality following cesarean section increased two in ten thousand deliveries. Section has been a factor in the reduction of the total mortality.

Peritonitis was the chief cause of death. It has been eliminated in the last three years by the use of the newer types of cesarean section.

Our faults have been high incidence and a lack of the proper selection of type of cesarean section in the contaminated cases. In the last



few years a better choice of operation has kept our mortality down in spite of the rise in the incidence of cesarean section.

These faults, high incidence and poor selection of type of cesarean section, are probably more or less common and doubtless largely account for the widespread high mortality following cesarean section.

The remedy, of course, is education of both the public and ourselves. It should be shown that cesarean section is not the simple, safe solution of the difficult labor that it is thought to be. We should equip ourselves well with obstetric surgery, both of the abdominal and vaginal varieties.

11 EAST FORTY-EIGHTH STREET.

(For discussion, see page 436.)

## THE USE OF SODIUM ISO-AMYLETHYL BARBITURATE (SODIUM AMYTAL) IN OBSTETRICS\*

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THE effort to alleviate pain by various procedures is about as old as civilization. The attempt to obtain painless childbirth has met with varying degrees of success. The barbituric acid derivatives have been used to a limited extent in obstetric practice in the United States but rather extensively in foreign countries to produce analgesia and surgical anesthesia.

In France, Fredet and Perlais<sup>1</sup> used allyl-isopropyl barbiturate (sommifene) to produce surgical anesthesia. A few years later, in Germany, Bumm<sup>2</sup> used a brom-propyl-phenyl replacement barbiturate, called pernokton, for the same purpose. L. Cleisz,<sup>3</sup> a Frenchman, who used sommifene (diethyl-allyl-iso-propyl-barbiturate of diethylamine) intravenously to abolish pain during labor, has reported 40 cases. Some work of this nature was done as early as 1923 in France. Cleisz administered a dose intravenously at two to three fingers' cervical dilatation and obtained perfect anesthesia for a period of ten hours. In his cases, he added pituitrin and used forceps to artificially shorten labor. In his conclusions he makes the statement that he considers it superior to any other form of obstetric anesthesia.

F. Delmas and A. Roume,<sup>4</sup> in their investigations, came to conclusions different from those of L. Cleisz. They used sommifene intramuscularly and intravenously in labor and were of the opinion: (1) that the child was sleepy and unable to nurse for several days following delivery; (2) that the restlessness of the mother was often extreme before, during, and following delivery; (3) that the mother slept several days; and (4) that the progress of labor was markedly impaired. They advised that the drug be employed circumspectly, confining it to hospital use.

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## EXPERIMENTAL WORK

Sodium iso-amylethyl barbiturate has been used extensively for the production of surgical anesthesia in animals.<sup>5</sup>

Page and Coryllos<sup>6</sup> found that the average minimum effective anesthetic dose in dogs was about 35 mg. per kilogram when given intravenously. Eddy<sup>7</sup> has shown that, in order to produce anesthesia in cats, 50 to 60 per cent of the lethal dose was required when administered orally and that the average fatal dose was approximately 100 mg. per kilogram of body weight. Swanson<sup>8</sup> found that in the routine intravenous administration of this salt for the production of anesthesia in animals (rabbits, cats, and dogs) a dose of 45 to 60 mg. per kilogram was necessary for operative procedures. Lundy and Osterberg<sup>9</sup> found amytal to be three times the strength of veronal, and Tatum and Parsons<sup>10</sup> found it the best barbiturate to use if survival of the animal was desired.

Sodium amytal was first used intravenously as a general anesthetic in humans in 1928 by McCallum;<sup>11</sup> he also found it was of value in the treatment of asthma, delirium tremens, and convulsions from various causes.

Zerfas and McCallum<sup>11</sup> observed that examinations of the urine, following the administration of the drug, were essentially negative except for excessive amounts of urates for twenty-four hours postoperatively. The CO<sub>2</sub> combining power showed no appreciable change during the anesthetic state. A slight drop in nonprotein nitrogen occurred for a day or two postoperatively but within normal limits. The blood sugar levels showed a tendency to increase, but rarely exceeded the maximum normal limit unless there was a previous metabolic disturbance.

The drug is prepared in a white crystalline form and is sealed in pyrex ampoules. A 10 per cent solution has been found satisfactory for intravenous use. The sterile triple distilled water is mixed with the sodium amytal by gentle agitation, and, as a rule, in one to three minutes a clear solution results. (If the solution is opaque for any reason, it should be discarded.) A freshly prepared solution is desirable; as chemical changes take place rapidly when the drug is dissolved in water, the mixture should not be allowed to stand for any great length of time.

The drug may be given orally, intramuscularly, or intravenously. When used intravenously in 10 per cent solutions, the rate of administration should not exceed one c.c. per minute. The patient drops off into what is apparently a normal sleep after 0.180 to 0.450 gm. (3 to 7 gr.) have been administered. Rarely does any excitement occur during injection of the drug.

The dosage varies according to the patient and the effect desired is based largely upon body weight, although individual variations are common. For surgical anesthesia, doses of from 0.015 to 0.025 gm. ( $\frac{1}{4}$  to  $\frac{1}{3}$  gr.) have been found satisfactory. For other purposes, 0.003 to 0.012-gm. ( $\frac{1}{20}$  to  $\frac{1}{5}$  gr.) per kilogram are effective.

## IN OBSTETRICS

The alleviation and abolition of pain during the progress of labor have been attempted in a multiplicity of ways. This fact alone indicates that success has been variable. Unlike general anesthesia for operative

procedures, a theoretically normal labor offers a very real problem in pain alleviation or abolition.

In a parturient woman, two lives are affected, and the active processes of labor must go to completion. Any means used to relieve or abolish the pains of labor must harm neither the mother nor the baby, and it must not interfere with the progress of labor to any appreciable degree.

#### EFFECT ON MOTHER

Sodium amytal has been used in more than 100 cases in our series. It has been administered in all stages of labor, orally, intramuscularly, intravenously, and rectally. It has been our desire to abolish the pain of labor or at least the remembrance of it.

We found very little slowing, if any, in the progress of labor. We had an apparent temporary delay in 4 cases, the longest being one hour. Uterine powers were impaired little, if any; however, voluntary

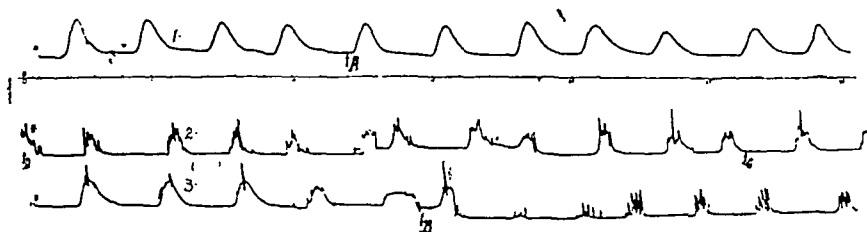
#### CHART 1

PARR I AGE 17 WT 50KG

HG MANOMETER

A GRAINS 4½ INTRAV  
B

C GRAINS 1½ INTRAV.  
D BAG IN VAGINA



powers in the first stages of labor were markedly diminished and the patient, at times, was unresponsive to uterine contraction. Voluntary powers in the second stage may be affected but not to any marked degree and not over thirty minutes. Even in obstetric anesthesia (or deeper) some patients continued powerful expulsive efforts when making no other voluntary move. One patient in the series seemingly had her labor stopped by a small dose of amytal, although she may have been having only false labor pains, or the drug may have been administered too early. Further use of the agent very early in labor will be necessary before conclusions may be drawn.

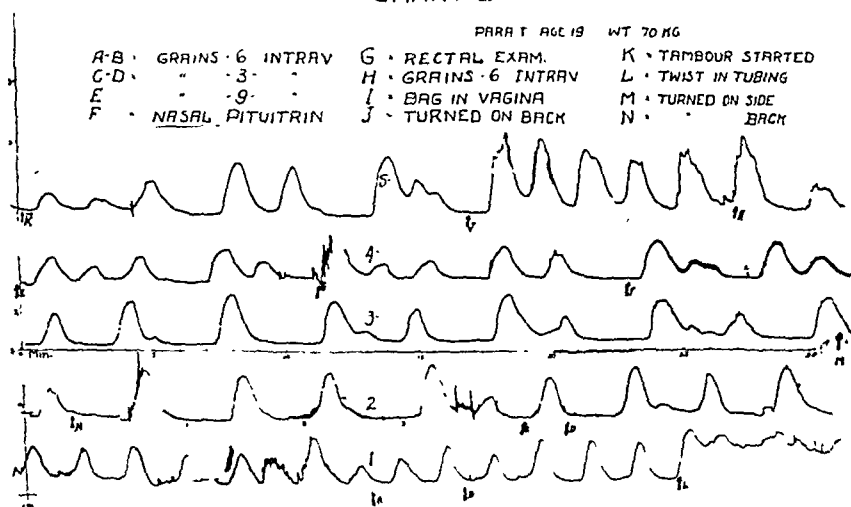
To measure the effects on uterine contractions, a mercury manometer was connected to a Voorhees' bag inserted in the cervix, and the contractions were recorded. Doses up to 0.018 gm. ( $\frac{1}{3}$  gr.) per kilogram were given within two hours without affecting the force, duration, or frequency of uterine contractions. (See Charts 1 and 2.)

In 28 normal cases of labor, the average time from the first injection of amytal until the delivery was three hours. The first injection was given when the uterine contractions occurred every four minutes and

when the cervix was partially effaced with two to three fingers' dilatation. The average time in a group of 12 primiparae was three and a half hours, while in 16 multiparae, the average time was one hour and fifty minutes. In this group of 28 patients, no patient delivered over six hours after the initial amytal injection. (See Table I.) The other patients who were given sodium amytal in normal labor were not detailed in the table as complete studies were not available.

In 80 patients, one-third showed no undue restlessness, one-third were markedly restless, and one-third were moderately so. (See Tables I and II.) There was no relation, however, between the degree of restlessness and the degree of amnesia. The patients occasionally cried out with labor pains, answered questions, asked for fluids, and yet remembered nothing of the parturition when questioned. Three patients had

CHART II:



perfect obstetric anesthesia until immediately after delivery of the baby, at which time they awoke and suddenly regained consciousness.

The restlessness occurred only with pains or because of an uncomfortable position and ceased with completion of the delivery. In the first stage of labor, the patients usually moved or complained with the labor pains and light restraints were necessary. In the expulsive stage it was necessary to restrain the hands to prevent disarrangement of the sterile drapings. The patients occasionally required forcible holding. The incidence and the degree of restlessness were greater when the drug was administered intramuscularly than when it was given intravenously.

No increase in postpartum bleeding was observed, and postpartum pains were probably decreased.

The maternal metabolic changes coincided with those of surgical cases,<sup>11</sup> having no variations outside of the normal limits. Urinary intake and output was in the normal ratio after delivery. The postpartum urine showed no unusual pathology.

TABLE I. THE SERIES OF CASES CHARTED ARE THOSE IN WHICH COMPLETE OBSERVATIONS WERE MADE UPON NORMAL LABORS. DURATION OF LABOR IS NOT INCLUDED AS IT IS UNCERTAIN

CASE NO.	PROGRESS WITH FIRST INJECTION†	DILATATION*	EFFACEMENT	TIME†† HR. MIN.	DOSE GRAINS	PARA	PAIN	RESTLESSNESS WITH DELIVERY
1	Q‡ 4 min. 60 sec.	II	Partial	2:15	12	VI	Slight	None
2	Q 4 min. 45 sec.	II	Partial	2:10	3½	II	Marked	Very
3	Caput visible			0:35	6	I	None	Slight
4	Q 4 min. 45 sec.	II	Partial	4:00	15	III	None	Very
5	Q 3 min. 60 sec.	III	Almost	6:00	7½	I	Moderate	Slight
6	Q 3 min. 60 sec.	IV	Complete	1:20	12	I	None	Very
7	Pain in Back	I	None	20:00	4½	I	Marked	Awake
**8	Q 3 min. 60 sec.	III	Partial	3:30	7½	I	Slight	Slight
9	Q 2 min. 60 sec.	III	Almost	0:30	12	III	None	None
10	Through cervix			0:30	12	I	None	None
12	Q 4 min. 60 sec.	IV	Complete	1:20	14½	II	None	None
13	Q 3 min. 45 sec.	II	Slight	3:00	18	I	None	Marked
**14	Q 3 min. 60 sec.	IV	Complete	5:00	10	I	None	Slight
15	Q 2 min. 60 sec.	III	Almost	0:40	5½	IV	None	None
16	Q 3 min. 60 sec.	IV	Complete	1:20	9	II	None	Slight
17	No engagement			8:10	15	IV	None	Moderate
18	Q 3 min. 60 sec.	IV	Complete	0:30	9	V	None	Moderate
19	Caput visible			0:05	7½	IV	Slight	None
20	Q 2 min. 60 sec.	IV	Complete	2:20	8	I	Slight	Marked
**21	Q 4 min. 60 sec.	IV	Complete	2:00	8	I	Moderate	Slight
22	Q 7 min. 60 sec.	I	None	12:00	20	I	Moderate	None
23	Q 2 min. 60 sec.	IV	Complete	1:00	9½	III	Slight	Slight
24	Q 10 min. 45 sec.	I	None	5:00	8	I	Slight	Slight
	(Irreg.)							
25	Q 5 min. 60 sec.	III	Partial	3:20	8	I	Moderate	Slight

\*Stated in fingers dilatation of the cervix.

†These patients had nitrous oxide and oxygen for episiotomy or repair.

‡Refers to frequency and duration of uterine contractions.

††From first injection of amnytal until delivery.

‡‡ (Quaque) meaning every.

There was no nausea, vomiting, or headache postpartum. Sleep, when present, varied in length up to six hours although the patient could be aroused for nourishment.

Sodium amytal, administered intravenously, in doses of from 0.003 gm. ( $\frac{1}{20}$  gr.) to 0.007 gm. ( $\frac{1}{9}$  gr.) per kilogram gave varying degrees of relief, but amnesia was not obtained. Doses of 0.007 gm. ( $\frac{1}{9}$  gr.) to 0.010 gm. ( $\frac{1}{6}$  gr.) per kilogram produced amnesia, and larger doses produced obstetric to surgical anesthesia. Women vary extremely in their pain thresholds and in their fortitude thus obviating a uniform dosage.

#### EFFECT ON BABIES

Fetal heart rates showed an average change of 10, the greatest variation being 30 and the least 5 per minute. The size of the dose bore no relation to the degree of variation. The fetal heart rate varied widely during labor over very short periods of time so that these variations were all within normal limits.

Of 80 babies studied in detail, 3 were asphyxiated, and breathing was started with more or less difficulty; 2 were apneic, while the remainder breathed spontaneously or with slight stimulation. (See Table II.) Their cries were forceful and no undue signs of depression were evident. One premature (seven and one-half months) baby was delivered, whose regular breathing started in three minutes. The mother was an eclamptic whose convulsions had been controlled for twelve hours with 48½ gr. of amytal given intravenously. (The last 15 grains were given for the operation.)

The average loss of weight in 30 babies was 9 ounces. The average time during which this loss occurred was three and five-tenths days. The average time in regaining their birth weights was eight and five-tenths days. (See Table II.) Four babies lost more than 12 ounces, 3 being forceps deliveries of primiparae. In our series of completely studied cases, one full-term baby, viable before delivery, was stillborn. No definite cause for the death was ascertained although it may have been due to an occult prolapsed cord.

\* \* \* \*

The intravenous injection of sodium amytal produced a marked sedative and analgesic effect beginning before completion of the injection and reaching its maximum in fifteen minutes. An intramuscular dose was approximately two-thirds as effective as a like intravenous one, was much slower in action, but was of longer duration. At the end of one hour, the intravenous effect began to wane. The intramuscular injection produced an effect in ten to fifteen minutes which reached its maximum in forty-five minutes and which began to wane after two hours. The dose was repeated as indicated. Pulses and blood pressures showed only variations consistent with normal labor and sleep.

TABLE II. THE SERIES OF CASES CHARTED ARE THOSE WHICH COMPLETE OBSERVATIONS WERE MADE UPON NORMAL LABORS. DURATION OF LABOR IS NOT INCLUDED AS IT IS UNCERTAIN

CASE NO.	AGE	WT. IN KG.	PARA	DOSE (GRAINS)	TIME UNTIL DELIVERY* HR. MIN.	AMNESIA	RESTLESS-NESS	TYPE OF DELIVERY	CONDITION ON DELIVERY	INFANT WT. LB. OZ.	WT. LOSS (OZ.)	DAY	WT. RE-GAINED
1	30	80	VII	12	2:15	Partial	None	L.O.A. Spon.	Crying	8-2	25	5	12
3	18	50	I	6	0:35	Complete	Marked	L.O.A. Spon.	Crying	7	9	5	-†
4	28	70	III	15	4:00	Complete	Marked	L.O.A. Spon.	Crying	7	7	4	11
5	18	60	I	7½	6:00	Partial	Slight	R.O.A. Spon.	Crying	5-14	4	2	5
6	17	55	I	12	1:20	Complete	Marked	L.O.A. Spon.	Crying	7	7	3	6
13	21	60	I	18	3:00	Complete	Marked	L.O.A. Spon.	Crying	7-4	19	3	-†
14	15	50	I	10	5:00	Complete	Slight	L.O.A. Spon.	Crying	7-5	6	3	7
15	22	50	IV	5½	0:40	Complete	None	L.O.A. Spon.	Crying	7-9	10	4	8
16	24	60	II	9	1:20	Complete	Slight	L.O.A. Spon.	Crying	9-9	12	4	12
17	24	70	IV	15	8:10	Complete	Moderate	L.O.A. Spon.	Crying	7-13	4	3	7
18	28	60	V	9	0:30	Complete	Moderate	L.O.A. Spon.	Crying	7-13	6	3	6
19	21	60	IV	9	0:05	Complete	None	R.O.P. Spon.	Crying	5-9	5	3	6
20	19	60	I	8½	2:20	Partial	Marked	L.O.A. Spon.	Crying	8	4	3	7
21	24	55	I	8	2:00	Partial	Slight	L.O.A. Spon.	Crying	6-6	8	4	6
22	30	65	I	20	12:00	Complete	None	SC.L.A. Spon.	Crying	7-7	9	3	9
23	23	60	III	9½	1:00	Partial	Slight	L.O.A. Forceps	Apneic	9-1	14	7	13
25	25	60	I	8½	3:20	Partial	Slight	R.O.P. Spon.	Apneic	7-3	3	3	6
**26	17	50	I	10½	5:00	Complete	Slight	L.O.A. Forceps	Apneic	7-11	5	2	5
27	16	90	I	19	2:20	Complete	Moderate	L.O.A. Spon.	Apneic	5-13	5	3	7
28	19	60	I	16	3:30	Complete	Slight	L.O.A. Spon.	Asphyxia	9-7	20	4	8
**29	17	50	I	10½	1:30	Complete	Slight	L.O.A. Spon.	Apneic	6-11	7	4	13
**30	14	60	I	11	10:00	Partial	Marked	L.O.A. Spon.	Crying	6-6	2	2	6
31	24	65	I	9	0:15	Complete	Moderate	L.O.A. Spon.	Crying	7	9	5	10
32	30	55	I	14	3:10	Complete	Slight	L.O.A. Spon.	Crying	5-10	4	4	7
33	19	70	I	25	6:30	Complete	None	R.O.P. Spon.	Crying	8-4	6	4	8
34	32	90	III	19½	2:40	Complete	Slight	L.O.A. Forceps	Crying	8-3	9	5	-†
						Complete	None	L.O.A. Spon.	Crying	6-4	1	5	6

\*From first injections of amnyal until delivery.

\*\*These patients had nitrous oxide and oxygen for epistiotomy or repair.

†Cases which had not regained birth weight on release.

## IN ECLAMPSIA

In eclampsia this drug offers immediate control of convulsions. Eight eclamptic convulsion cases have been treated and in every instance the convulsions were immediately controlled.

## CASE REPORTS

One case, a primipara, aged eighteen, continued to have convulsions for one and one-half hours after having received one-half grain of morphine. Further convulsions, however, were controlled by moderate doses of sodium amytal. Two hours later a stillborn female was delivered by forceps. Two hours postpartum this patient had another convulsion; amytal was administered, and an uneventful recovery occurred.

The second case was that of a patient who was having convulsions in rapid sequence. Six grains of sodium amytal controlled them. The patient died three hours later, and the postmortem examination showed a beginning lobar pneumonia.

The third patient had three convulsions in an hour. Eleven grains of sodium amytal were administered and no further convulsions occurred. It was repeated at intervals of an hour or more. Twelve hours following convulsions, a cesarean section was done under 15 gr. of sodium amytal (making a total of 48½ gr. in twelve hours) and a living seven and one-half months' baby was delivered with no undue respiratory depression. No more sodium amytal was given. The patient died of cardiac collapse on the second postoperative day.

The fourth case, a colored primipara, entered the hospital apparently moribund following three convulsions in the home. She showed all the signs and symptoms of eclampsia. Morphine was given and, after two convulsions, 5 gr. of sodium amytal were administered intravenously. She had a slight convulsion two hours later. The intravenous injections were given when she began to be markedly restless. She was given 25 gr. intravenously and 60 gr. intramuscularly over a period of three days until the fear of convulsions was over. Five days later she delivered a dead fetus. Blood pressure during convulsions varied from 178/110 to 140/100. Moderate decreases in blood pressure were observed during the time of injection though shortly after it returned to its previous level. Except for the administration of sodium amytal, the usual treatment was employed. The patient was released after six weeks hospitalization in fair condition, with a blood pressure of 138/70 and with no pathologic urinary findings.

A fifth case of eclampsia, considered by many consultants to be moribund, was treated for five days with the usual methods without favorable results. A cesarean section was done, using sodium amytal intravenously for anesthesia, with an uneventful recovery.

A sixth eclamptic was satisfactorily anesthetized for cesarean section and was delivered of twins, all three patients surviving.

The seventh and eighth cases were postpartum eclamptics whose convulsions were entirely controlled by the use of sodium amytal. Both recovered.

The typical case of eclampsia having convulsive seizures was treated as follows: Sodium amytal 0.500 gm. (7½ gr.) was administered intravenously, which dose was usually sufficient to control the convulsions; some cases, however, required as much as 0.8 gm. (12 gr.) as the initial dose. Four or 5 subsequent doses were given by combined intravenous and intramuscular administration, steadily reducing the intravenous dose. By the sixth dose the administration was usually entirely intra-



muscular. Following the initial dose, 0.5 gm. ( $7\frac{1}{2}$  gr.) was usually sufficient. The repetition of the drug depended entirely on the restlessness and the recurrence of the convulsions. Careful observation of individual patients may best serve as the guide for their treatment, as no fixed rule relative to dosage or repetition of the injections can be made.

#### IN CESAREAN SECTIONS

Eleven cesarean sections have been done under sodium amytal anesthesia; in a few instances it was necessary to supplement this anesthesia with nitrous oxide and oxygen. Four patients, a proved nephritic with hypertension, an aortic aneurysm, a toxemia of pregnancy, a pre-eclamptic and a placenta previa in a state of shock, all made uneventful recoveries. An eclamptic in a moribund state, following control of convulsions, died two days postoperative from cardiac collapse.

In each of the 11 cesarean sections, the uterus showed no signs of atony, and contraction took place promptly. In one case, when pituitrin was given, the uterus contracted so firmly that it rendered closure of the incision difficult.

#### MISCELLANEOUS CASES

Two advanced cases of tuberculosis had labor induced by the hydrostatic bag under sodium amytal anesthesia. Both survived and were later discharged to tuberculosis institutions.

One patient, who was very ill from the effects of a large renal calculus, had labor induced by the bag method under this anesthetic and made a good recovery.

One patient, five days after delivery, was given 15 gr. of sodium amytal intravenously as the only anesthetic for a rib resection for empyema; she made a rapid recovery. Four cases of hysterotomy and sterilization were done under this anesthetic, and the patients all made good recoveries. In 6 patients it was used as the anesthetic in the removal of secundines from the uterus.

Many other minor operations such as episiotomies, perineorrhaphies, dilatations, and curettements, were done under sodium amytal anesthesia. In some instances the dose given was not adequate to produce satisfactory anesthesia so that small amounts of nitrous oxide were required.

#### DISCUSSION

Analgesia and anesthesia in obstetrics are justly entitled to consideration, and, though this work is new and incomplete, it merits further study. The foreign work done in this field has brought forth conflicting statements with the preponderance favorable to the urea compounds. The variations in their results may be explained on the basis of the instability of the drug in solution with improper buffering. This disadvantage has been largely corrected in the preparation of sodium iso-amylethyl barbiturate in its present form.<sup>14</sup>

In our cases, the best procedure in the average 125-pound woman was:  $\frac{1}{8}$  to  $\frac{1}{6}$  gr. of morphine,  $\frac{1}{150}$  to  $\frac{1}{200}$  gr. of scopolamine and of intramuscular amytal 0.390 to 0.585 gm. (6 to 9 gr.) when contractions

were regular and were occurring in less than ten minute intervals. The injection of sodium amytal was repeated as indicated. An intravenous injection was usually given at the beginning of the second stage in amounts from 0.390 to 0.650 gm. (6 to 10 gr.). It was administered slowly during several pains, stopping when the patient was well controlled. In some instances the patient's arms and legs had to be restrained in order to avoid disarrangement of the draping.

In most of the cases reported in this paper, the intravenous method of administering the drug was used. By this method we were better able to control the dosage and to make accurate observations. Also, the effects of the drug were rapidly obtained.

As a preliminary report, we feel justified in drawing the following conclusions:

(1) The most serious objection to the use of sodium amytal as an analgesic was the difficulty in controlling the patients who became very restless. (2) This drug has the advantage of being rapid in its action and of having a wide range of safe dosage. (3) There has been no evidence of harm to the mother. (4) Labor is probably not delayed. (5) Labor may be rendered practically painless. (6) Obstetric operative procedures are much more easily carried out under ordinary anesthetics when the operation is preceded by sodium amytal. (7) Danger to the baby has not been proved. (8) Prompt and complete control of eclamptic convulsions is possible. (9) As a general anesthetic agent for cesarean sections and other obstetric operations and especially for patients having tuberculosis or toxemia of pregnancy, sodium amytal bids fair to supplant the inhalation anesthetics.

We are deeply indebted to Doctor H. F. Beckman, Doctor Foster Hudson, Doctor D. L. Smith, Doctor C. O. McCormick, and other members of the Obstetrical Staff of the Indianapolis City Hospital and the Coleman Hospital for Women.

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## CAUDAL ANESTHESIA IN OBSTETRICS

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WHILE working with Samuel H. Cosgrove at the Jersey City Hospital, Jersey City, New Jersey, on spinal anesthesia in obstetrics, I conceived what I felt might be an ideal labor anesthesia. I was interested in normal spontaneous deliveries, and not in operative cases, as we had developed the handling of spinal work to a point of efficiency for abnormal cases where we were extremely pleased with its results when a general anesthesia was contraindicated. My plan was to make free use of morphine and rectal analgesia for the first stage and complete the delivery under caudal anesthesia. I used this method in 34 cases, which is rather a small series, I admit, but large enough to warrant drawing logical conclusions.

The technic of giving a caudal anesthesia to a woman in active labor is of course more difficult than when administered to a thin surgical patient whose mental excitement has been greatly reduced by sedatives. The time of administration was exceedingly difficult to determine, but we tried to give it to the multiparae late in the first stage when we thought delivery would be completed in one hour, and to the primiparae when the cervix was completely dilated and the caput beginning to show. If the patient was placed in the knee-elbow position, she complained bitterly, seemingly due to the weight of the fetus against the pelvic structures. We therefore concluded it was much easier and more satisfactory to give the novocaine with the patient on her side, her thighs flexed on the body, but even then it was technically difficult, on account of her movements during a pain. This was especially so in the case of patients with a tendency toward obesity. In three patients the hiatus could not be found due to excess adipose tissue, in another on account of a deformed sacrum in a rachitic negress.

Of the remaining 30 cases, 15 were successful and 15 failures. This classification was made on a basis of an anesthetic for spontaneous deliveries only. In the 15 successful cases, 7 were primiparae and 8 multiparae. These women I am sure had painless deliveries as far as the birth of the head over the perineum was concerned. However, most of them complained of the abdominal uterine pain which is apparently almost as distressing as the perineal pain. One nineteen-year-old-primipara delivered a six-pound baby and was surprised to know it had been born, having experienced no pain whatsoever. A para ii stated she felt the baby's head being born, but that there was no pain. Another para ii said that having babies would not be such an ordeal if they could all arrive under similar conditions. All patients were very grateful for the relief.

In the 15 unsatisfactory cases 8 were multiparae and 7 primiparae. One multipara was delivered by the intern while I was preparing to give the caudal anesthesia. Another was delivered immediately after the anesthesia had been given. The ten or twelve minutes necessary for the onset of anesthesia had not elapsed in this case. Another para ii stated that she had far more pain with this baby than with her first which was also a spontaneous delivery. I was unable to demonstrate perineal anesthesia in that case. Another primipara obtained absolutely no relief, and no anesthetized area could be demonstrated. In these 2 cases 50 c.c. of  $\frac{1}{2}$  per cent novocaine solution was used.

A much greater fault to be found with the anesthesia than the inability to time it correctly, is the inertia it produces. Practically every patient developed some degree of inertia. Out of the 30 cases there were 5 complete inertias. Five more cases had a marked reduction of pain, and of these 8 necessitated forceps for completion of the delivery. Only a few whiffs of ether were necessary in the partial cases and none in the complete inertias except one. This case was allowed to go three hours, and although the inertia still existed, the anesthesia had disappeared some time before. The ratio of lacerations was about the same as our other cases where inhalant anesthetics were used. The two episiotomies and the lacerations were repaired without further anesthesia.

The toxicity of the drug used is a very noteworthy factor and one to which I had given but little thought at the beginning of these observations. When the injection was made too rapidly, temporary central nervous disturbances were encountered, which manifested themselves by sudden headaches, dizziness, hallucinations, disorientation, and emotional instability. Likewise, the blood pressure and pulse frequently fluctuated, increasing in some and decreasing in others, and not infrequently cardiac pain occurred. Although these disturbances were minimized by very slow injections, they also occurred when no fault in technic could be found. Furthermore, it had a definite toxic effect on the baby. Whether this occurred only when used following rectal analgesia and morphine, I am not ready to say. One patient developed a slowing of the fetal heart twenty minutes after the administration. The fetal heart continued to decrease, the fetus became very active and the heart tones were lost. A forceps extraction was done, during which time the mother slept soundly, with the delivery of a stillborn baby. Autopsy failed to show any cause of death. This patient had had a rectal analgesia nine hours before the caudal was given. Another patient, where 60 c.c. of  $\frac{1}{2}$  per cent novocaine were used, developed a complete inertia and slowing of the fetal heart fifteen minutes after injection. The fetal heart went down to 50, became very irregular and the fetus became very active, but it regained its normal rhythm ten minutes later, following the injection subcutaneously of 3 minims of

adrenalin. She had been given analgesia three hours before the caudal. I am unable to explain these two cases in any other way except from toxic absorption. However, I have inquired of others who have used local infiltration of novocaine for cesarean sections, but they can always account for their stillbirths by more definite causes. I saw a decompensated cardiac patient sectioned under local infiltration anesthesia whose baby was never resuscitated, although the heart was good at delivery. The mother had had a great excess of morphine in an attempt to stabilize her heart, which could readily explain the cause of the stillbirth. Dr. Schellekens had one stillbirth out of 6 cases, the one occurring after a prolonged insignificant first stage; the patient was delivered one hour after the injection of 20 c.c. of 2 per cent procaine. However, he did not believe the death was due to the drug.

After making a careful study, the dosage used was altered both in amount and strength from 30 to 60 c.c. of  $\frac{1}{2}$  per cent and 1 per cent novocaine, and very little difference was noted. The number of severe inertias was slightly reduced with  $\frac{1}{2}$  per cent, but complete ones did occur and the fetus almost expired when this strength was used. The effect was more uncertain with the weaker solutions. We do not believe in the use of pituitrin intrapartum, so the use of this drug to overcome these inertias was not tried. I was interested only in an anesthesia for spontaneous deliveries, per se, and not for operative cases because we had a more certain anesthesia in our intraspinal injection of soluble novocaine crystals when an inhalation anesthesia was contraindicated.

From these 34 cases, where there were four failures to find the hiatus and only half of the remaining cases were successful, the following conclusions may be drawn:

1. The administration of caudal anesthesia in obstetrics is technically difficult and results are not uniform. It should be given only under the strictest precautions and therefore cannot be used in the average home delivery.

2. There is difficulty in timing its administration, since it is often given too late in multiparae and too early in primiparae.

3. Caudal anesthesia produces a certain amount of inertia in practically every case, from a very slight reduction to a complete abolishment of the uterine contractions, necessitating operative deliveries for the completion of the labor.

4. It produces definite toxic manifestations in the mother and, with but little question, is the cause of fetal distress.

5. It does not relieve the pain from the uterine contractions when an inertia does not develop. Since these pains are apparently almost as distressing as the pain from the delivery of the head over the perineum, adequate relief is not obtained for the patient.

6. In the light of these conclusions caudal anesthesia is not satisfactory for spontaneous deliveries.

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1115 MEDICAL ARTS BUILDING.

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A STATISTICAL STUDY OF THE INCIDENCE OF CONTRACTED PELVES IN CHINESE WOMEN AND ITS RELATION TO LABOR AND THE SIZE OF THE NEWBORN

BY SUSANNE R. PARSONS, M.D., LOS ANGELES, CAL.

THIS study of the pelves of Chinese women was undertaken in order to ascertain, if possible, whether the measurements usually accepted as normal for other races, would apply to the Chinese. Accordingly, in a series of 500 women who were delivered spontaneously at the Margaret Williamson Hospital, Shanghai, the pelvis was measured and the data were recorded as to age, parity, presentation, length and weight of the child, and its head measurements. No attempt has been made to use the duration of labor as a factor in this study because of the uniformly unreliable histories obtained. Since the patients were rarely seen before the onset of labor, the pelvic measurements were made at the postpartum examination in maternity, before the discharge from the hospital. The measurements taken were the iliac spines and crests, the trochanters, Baudeloeque's diameter, the diagonal conjugate and the transverse diameter of the outlet, and for the sake of uniformity I made all these measurements.

Similar data were recorded in a series of operative cases, but unfortunately the number in which complete data were obtainable is very small (83), on account of the propensity of sick Chinese patients to run away from the hospital before being discharged and the failure of the hospital to prevent this practice.

In spite of a careful search through the literature no adequate measurements of the Chinese pelves were found. Garner<sup>3</sup> has measured a number of Chinese pelves but failed to include measurements of the trochanters and diameter of the outlet. As a result she erroneously concludes, "—there are yet few cases of contracted pelves among them." Whitmore<sup>4</sup> makes the same error. Oppenheim (Fukien<sup>1</sup>) gives the average weight of newborn Chinese infants as 3225 gm. for 441 males and as 3094 gm. for 501 females. No lengths or head measurements were given. It seems fair to assume that the pelvic measurements in our series may be taken as a representative average for Chinese women,

since the patients seen at Shanghai are drawn from all parts of China and comprise the larger northerners as well as the smaller southerners.

In this series of 500 spontaneous deliveries the pelvic measurements show the following averages: spines 22.07 cm., crests 26.56 cm., trochanters 29.31 cm., Baudelocque's diameter 18.80 cm., tuber ischii 8.53 cm. In only 159 of the cases was the diagonal conjugate reached and in them it averaged 11.60 cm. In all others it may be assumed to be approximately normal and to measure 12 cm. or more. In other words, the average measurements fall far below the standards regarded as normal for European and American women.

If the classification of Michaelis and Litzmann is taken, except for the funnel pelvis where a distance between the tuber ischii of 8 cm. or less is used (Williams), we find that the cases in our series fall into three main groups, funnel, generally contracted funnel, and generally contracted, as shown in Table I. There was a striking absence of rachitis, and I saw only three definite cases of rachitic pelvis in the course of over 1,500 pelvic examinations.

TABLE I. INCIDENCE OF PELVIC CONTRACTION AND PERCENTAGE OF VARIOUS TYPES OF CONTRACTION

	SPONTANEOUS	OPERATIVE
Contracted pelvis	249, 49.8%	48, 58.5%
Funnel typical	160, 32.0%	25, 30.4%
Generally contracted	60, 12.0%	11, 13.4%
Generally contracted funnel	29, 5.8%	12, 14.6%
PERCENTAGE OF TOTAL NUMBER OF CONTRACTED PELVES		
Funnel typical	64.25%	52.0%
Generally contracted	24.09%	22.9%
Generally contracted funnel	11.6 %	25.0%

One notes at once the high incidence of contracted pelvis (49.8 per cent) found in 500 women able to deliver themselves spontaneously, and particularly the high incidence of funnel pelvis (32 per cent) in the series, which means that the latter constitutes 64.25 per cent of all contractions encountered. The fact, moreover, that Emmons<sup>2</sup> reported an incidence of 9.2 per cent funnel pelvis among 217 North American Indian squaws is of anthropologic interest as a possible additional point connecting these two races.

Table II shows the comparative frequency of the several types of contracted pelvis in the white, black, and Chinese races, the figures for the first two races being taken from Williams and Sun.<sup>5</sup>

From Tables II and III it will be seen that the incidence of contraction among Chinese women is nearly 3½ times as great as among white women in Baltimore and is slightly greater than among black women in that city. The funnel type of contraction occurs 6 times more frequently than among the whites, about 5 times more frequently than

among the blacks, and  $3\frac{1}{2}$  times more frequently than among the North American Indians.

The tables also show the preponderant position which the funnel pelvis occupies in Chinese women, in whom it makes up 64.25 per cent of all abnormal pelves, as contrasted with 33.49 per cent and 12.87 per cent respectively in the white and black women of Baltimore. In other words, it more than takes the place of the generally contracted and generally contracted rachitic pelves seen in patients in that city.

TABLE II. COMPARATIVE FREQUENCY OF DIFFERENT TYPES OF CONTRACTED PELVES ACCORDING TO RACE

PELVES	WHITE (PER CENT)	BLACK (PER CENT)	CHINESE (PER CENT)	N. AM. INDIAN (PER CENT)
Generally contracted typical	4.74	16.62	12.0	
Generally contracted funnel	0.64	4.31	5.8	
Funnel typical	5.03	6.44	32.0	9.2
General rachitic	0.52	14.21		
Simple flat	2.43	0.84		
Flat rachitic	0.30	1.02		
Total	13.66	43.44	49.8	9.2

TABLE III. PERCENTAGE OF DIFFERENT TYPES OF CONTRACTED PELVES ACCORDING TO RACE

PELVES	WHITE (PER CENT)	BLACK (PER CENT)	CHINESE (PER CENT)
Generally contracted typical	35.23	38.80	24.09
Generally contracted funnel	4.75	10.06	11.6
Typical funnel	33.49	12.87	64.25
Generally contracted rachitic	3.82	33.17	
Simple flat	18.07	1.96	
Flat rachitic	2.20	2.37	
Atypical	2.43	0.76	

In order to make our data on pelvic measurements of practical obstetric value, an attempt has been made to correlate it with the data on the size of the newborn. For this purpose the weights of 1000 full-term infants delivered at Margaret Williamson Hospital just prior to my service there, were averaged and found to be 3123.73 gm., or 126.27 gm. less than the average for white infants. The average weight of the newborn infants in my series of 500 cases was somewhat less or 2958.61 gm. It seems this average may be low, since it includes only spontaneously delivered infants.

TABLE IV. LENGTH AND WEIGHT IN THE NEWBORN

	WHITE	BLACK	CHINESE
Length	49.64 cm.	48.75 cm.	50.16 cm.
Weight	3316.9 gm.	3104.8 gm.	2958.61 gm.

The average length of the full-term, newborn Chinese infant as obtained from our 500 spontaneous cases is 50.16 cm., as compared to



49.64 cm. for white infants and 48.75 cm. for black infants (Williams) Table IV. Unfortunately no record of the length or head measurements was made in the 1000 cases referred to above. The head measurements of these 500 infants (FO 11.56 cm., MO 13.20 cm., BP 9.16 cm., SOB 9.58 cm., SOB circumference 30.92 cm.) show no striking variations from normal, Table V.

It would appear from Table IV that the average Chinese baby born in Shanghai falls below the usual average, which may account for the relative ease of labor.

TABLE V. HEAD MEASUREMENTS OF NEWBORN

	AVERAGE (CM.)	WHITE (CM.)	BLACK (CM.)	CHINESE (CM.)
FO	11.75	11.71	11.26	11.56
MO	13.5	13.33	13.31	13.20
BP	9.25	9.25	9.05	9.16
SOB	9.5	9.7	9.29	9.58
SOB circ.	32.0			30.92

In view of the fact that among whites and negroes the smaller infants are found in cases of generally contracted pelves and the larger children in typical funnel and simple flat pelves, a modal study of the weights found in each of the three types of contraction encountered among the Chinese was made and is shown in Table VI. It will be seen that in the funnel typical pelvis, 38 per cent of the infants weigh

TABLE VI. MODAL WEIGHTS OF NEWBORN INFANTS GROUPED ACCORDING TO OCCURRENCE IN DIFFERENT TYPES OF Pelves

	TOTAL SERIES (PER CENT)	FUNNEL (PER CENT)	GEN. CONTRACTED (PER CENT)	GEN. CONTRACTED FUNNEL (PER CENT)
Less than 2500 gm.	9.73	10.0	5.0	0.0
2500 - 2999	31.33	38.1	21.6	20.6
3000 - 3249	22.6	20.6	30.0	37.9
3250 - 3499	19.0	16.8	18.3	13.7
3500 - 3749	9.2	8.7	15.0	17.2
3750 - 3999	6.6	4.3	5.0	10.3
4000 - 4499	1.0	0.0	3.0	0.0
4500 or more	0.05	0.0	1.6	0.0

2500-2999 gm. In the generally contracted typical pelvis, 30 per cent of the infants weigh 3000-3249 gm. In the generally contracted funnel, 37.9 per cent of the infants weigh 3000-3249 gm. In this group also are found more infants between 3500 and 3999 gm. Thus, we see quite the reverse condition obtains in the weights of Chinese infants, i.e., among generally contracted pelves 33.3 per cent weigh 3250-3749 gm., while among the generally contracted funnel 30.9 per cent weigh 3250-3749 gm., and among the funnel pelves 25.5 per cent weigh 3250-3749 gm.

If we admit that the generally contracted pelvis is a stigma of degeneration, and consequently smaller children are born of these women, we are confronted by the fact that either this does not hold true in the Chinese, or these pelves are not true examples of general contraction. In view of the high percentage of contracted pelves occurring in a series of spontaneous deliveries, and the uniformity with which the measurements as a whole fall below the accepted average for whites and the fact that the larger infants occur in the group of generally contracted pelves, it would seem that we are justified in assuming that the normal measurements for a Chinese female pelvis fall below the accepted standard of other races. Therefore this mode should be determined for the guidance of the obstetrician. Further compilation of data on the size of newborn infants, careful pelvic measurements, and type of labor will be necessary, however, before this can be finally established.

In order to establish the part played by age and parity of the mother and presentation of the child in determining the type of labor, a study was made of these factors and the results were what would be expected in any series of obstetric cases. In examining the presentations which occurred in the operative cases, an unusual number of transverse, 18.07 per cent was noted, as well as 8.43 per cent compound presentations.

I am fully aware that this series of cases is small and inadequate as a basis for establishing authoritative data on labor in Chinese women, but it is presented with the hope that even this compilation of measurements may be of assistance to the obstetrician dealing with Chinese patients. It is hoped even more that it may stimulate workers now in China to keep more careful and complete obstetric records for future compilation and analysis.

#### SUMMARY

The average pelvic measurements of 500 Chinese women delivered spontaneously in Margaret Williamson Hospital, Shanghai, show that they fall below the usual standards.

In this series 49.8 per cent of the pelves were abnormal, and the typical funnel pelvis accounts for nearly two-thirds of the entire number, while rachitic and simple flat pelvis did not occur.

It is with pleasure that I acknowledge the kindness of Dr. J. Whitridge Williams, Johns Hopkins Hospital, for his invaluable suggestions and criticism of the data here presented.

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## ANEMIA IN PREGNANCY

### A PRELIMINARY REPORT ON ONE HUNDRED OBSERVED CASES

BY JOHN H. MOORE, M.D., F.A.C.S., GRAND FORKS, N. D.

THIS report is based on a study of one hundred pregnant women who consulted me between January 1, 1928, and August 1, 1928. Its purpose was to determine the average hemoglobin percentage and red blood cell count in a group of unselected cases seen consecutively in my private obstetric practice.

No attempt was made to classify these cases as to period of gestation. While the majority came for prenatal care during the first or early second trimester, a number did not appear until well along in the third trimester and one patient was not seen until labor was imminent.

All of these patients were white, in from moderate to good circumstances, and represented a fair cross-section of the childbearing population of this agricultural community.

#### PROCEDURE

At the first examination each patient's history was taken, and physical and laboratory examinations were made. These included a urinalysis, hemoglobin determination with the Dare hemoglobinometer, red blood cell count, and a blood Wassermann test on every patient. All the hemoglobin determinations were made by the same trained observer and the figure taken was the average of three consecutive readings. This same technician made all the red blood cell counts and the results are shown in the accompanying tables.

TABLE I

NUMBER OF CASES	AVERAGE HG.	AVERAGE R.B.C.
100	77.7%	4,140,675

TABLE II

	NUMBER OF CASES	AVERAGE HG.	AVERAGE R.B.C.
Primiparae	52	76.8%	4,160,145
Multiparae	48	78.6%	4,121,205

Five patients in this series had nephritis as a complication in pregnancy; 3 were primiparae and 2 were multiparae. The average hemoglobin in this group was 55 per cent, and the average red blood cell count, 3,375,250. It was in this group that the lowest readings were found: There was an octipara with a hemoglobin reading of 35 per

cent and a red blood cell count of 1,520,000. Her case was further complicated by mitral stenosis. This unquestionably hastened her death on the third postpartum day.

Three patients in this series had syphilis. In 2 of them the blood Wassermann reaction was 4-plus and in the third, a primipara with interstitial keratitis, the first reaction was 1-plus but under provocative treatment it became 4-plus. The average hemoglobin for this group was 76.6 per cent and the average red blood cell count was 3,760,000.

One patient, a primipara with mild diabetes mellitus, had a hemoglobin reading of 76 per cent and a red blood cell count of 3,750,000.

For purposes of comparison this series of 100 cases is further divided into hemoglobin groups in Table III.

TABLE III

	50 OR LESS	50-60	60-70	70-80	80-90	90 OR ABOVE
Number of cases	3	4	12	31	39	11

The maximum hemoglobin reading was 94 per cent and occurred in a multipara. She had a red blood count of 4,900,000.

The maximum red blood cell count of the series, 5,980,000 also occurred in a multipara. She had a hemoglobin reading of 85 per cent.

#### CONCLUSIONS

1. No wide variation exists between multiparae and primiparae in either hemoglobin readings or red blood cell counts in this series.

2. The nephritic group showed a substantial reduction in both hemoglobin and red blood cells over the general average.

3. The syphilitic group showed a lower average in red blood cells than the average red blood cell count of the series, but with practically no change in the hemoglobin average from that of the entire series.

I am indebted to Mrs. Helen G. Korstad, laboratory technician, for the hemoglobin determinations and red blood cell counts on all the patients in this series.

NORTHWESTERN NATIONAL BANK BUILDING.

# ON THE CONTROL OF EPIDEMIC IMPETIGO NEONATORUM BY MEANS OF GLYCERINE

BY ELLIS KELLERT, M.D., SCHENECTADY, N. Y.

(From the *Ellis Hospital*)

**N**O MORE annoying condition is encountered by the obstetric departments of hospitals than the occasional invasion of the nursery by impetigo contagiosa.

Several references in the literature show that there is a well established basis for the use of glycerine in treating infection and inhibiting bacterial growth. Since at best it is but mildly antiseptic and requires prolonged contact for favorable effect, glycerine must of necessity have limited applications. My object is to call attention to a simple method for the prevention of a contagious skin disease—impetigo contagiosa.

In February, 1927, our attention was called to the presence of impetigo in the Ellis Hospital nursery. Despite all precautions, isolation, and special nurses, the disease spread from one infant to another. Mercurial ointment and mercurochrome were in constant use but with little influence on the spread of the infection. Invariably more than one bleb developed and in some instances the disease approached a bullous form. The method proposed and apparently used successfully was to anoint the entire body of each infant, after its bath, with a solution consisting of equal parts of glycerine and water.

This procedure is based on the fact that 50 per cent glycerine inhibits the growth of pyogenic cocci and is not irritating to the skin. The thin film of glycerine on the skin appears to retard the growth of bacteria sufficiently to prevent the lesions from developing. No irritation was noted as resulting from the use of the glycerine. The solution of 50 per cent or 60 per cent glycerine should be kept in a stock bottle sterilized by boiling or in the autoclave. In using the solution, it should be poured from the bottle on cotton and daubed over the skin, nails, scalp, etc., following the bath.

When the treatments were begun there were 16 babies in the department, four of which had the disease in varying degrees. Two of the more extensively affected infants were removed from the hospital. The remaining two were sponged daily with the 50 per cent glycerine solution and likewise the 12 normal infants. Of the former no new lesions appeared and of the latter none developed the disease. Apparently the epidemic ceased.

In November, 1927, one infant in the nursery developed characteristic blebs near the right axilla and a diagnosis of impetigo was made. The glycerine method was immediately instituted and kept up for four days, twelve infants being so treated. No further cases developed nor did

the disease spread in the infant affected. This is the first time in recent years that the disease was limited to one patient. During the year 1928 impetigo appeared twice. On each occasion all infants in the nursery were sponged daily for four days with the glycerine and no additional cases developed.

Our experience with the method, while not establishing its value conclusively, is such as to recommend its use in the absence of a more effective method. Even when the water-baths are omitted for a week and glycerine used alone the skin is less irritated, more supple and healthier appearing than under the usual nursery routine. Should an epidemic prove refractory to the 50 per cent glycerine it is urged that a 60 per cent mixture be used but it is doubtful that a stronger solution will prove more effective.

Since we have been free from epidemics of this disease for some time now, this preliminary report is made with the hope that the method will be tried elsewhere for apparently the disease is quite common throughout the country and difficult to eradicate completely.

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## NOTE ON THE FORMATION OF AN ARTIFICIAL VAGINA

BY STEPHEN RUSHMORE, M.D., BOSTON, MASS.

**I**N THE AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY for December, 1927, Frank and Geist describe an operation which is an adaptation of the pedicled tubular skin flap used with such remarkable success by Gillies and described in his work on *Plastic Surgery of the Face*. Frank and Geist used a single skin flap from one thigh, but suggest the possibility of using a flap from each thigh. There is herewith reported a case in which this suggestion was followed, with satisfactory anatomic result.

The patient (aet. 23) was first seen in the spring of 1927. She had a severe attack of pneumonia at fourteen, about the time it was expected that menstruation would appear. General health good. No pelvic symptoms. Patient has never menstruated nor has she had any menses at any time. No bladder nor rectal symptoms. The patient is in apparently very good general health. Face of feminine type. No suggestion of beard, very slight down on upper lip. Thyroid cartilage perhaps rather prominent. No enlargement of thyroid gland. Body form of female type. Axillary hair development slight. The abdomen is normal. Escutcheon, feminine type, well developed. There is a slight prominence in each groin, due to a small subcutaneous tumor, which is movable, slipping down easily into the labium majus, but not upward into the abdominal wall. The inguinal canal is present, but shows no definite hernia. These tumors are about the size of normal ovaries, and are not tender. There is a hypertrophy of the labia majora which are fairly abundantly covered by dark hair (patient, brunette) and meeting in the median line so that subjacent parts posteriorly are not visible until labia are separated; but anteriorly the clitoris is visible, hypertrophied, with glans not covered by prepuce, about three-eighths of an inch in diameter.

On separating the labia majora, folds comparable to labia minora are very slight. In a depression the urinary meatus is visible, and posteriorly is another slight depression. No hymen can be made out. The posterior depression just admits tip of finger and on introducing a probe proves to be about half an inch in depth. Rectal examination showed no evidence of vagina, of uterus, nor of ovaries in the pelvis. No tumor in pelvis.

The patient stated that she wanted to get married and sought advice. Operation was not urged, and the patient left the office to think the matter over for the summer.

The patient returned July 20, 1928 and desired operation. The procedure was carried out in two stages, July 24 and September 29, 1928, the patient going home between the operations, and leaving the hospital finally in the third week in October.

The type of operation was that described by Frank and Geist, employing the modification suggested by them, of using a tubular flap from each thigh, instead of a single flap from one thigh.

The base of the flap was two inches from the median line; the flap was about two inches wide, and five inches long. The skin of each flap was dissected free (except at the ends), some of the subcutaneous fat cut away and a solid tubular flap formed by suturing the skin edges. The skin of the thigh was then under-cut and the edges approximated under the flap. The flaps healed perfectly except for slight inaccuracy of approximation of skin edges, from not cutting away quite enough fat. There was cutting in of the stitches in the underlying skin, and superficial infection, from too much tension, although it did not seem too great when the stitches were placed. The difficulty in healing, from these two factors mentioned, was a marked tendency of the underside of the tubular flap (line of suture) to adhere to the underlying granulation tissue. This presented however, no serious trouble. The circulation of the tubular flaps was always good.

The second stage of the operation was performed about two months later, September 29, 1928. A transverse incision was made near the posterior margin of the depression posterior to the urethra, and carried out about an inch on each side. This incision was gradually deepened, carrying it between urethra and bladder and the rectum until the peritoneum was reached. There was considerable bleeding which was pretty well checked by tying and by passing sutures and by packing with iodoform gauze.

The left flap was then cut free at its distal end, laid open along the line of original incision and trimmed of excessive fat and scar tissue. The transverse incision was then carried out along the anterior side of the base of the flap and around the base and posteriorly for about an inch and a half. The flap on the right side was freed in a similar manner, and then the two flaps sutured in the median line to form the new vagina, lined by skin and covered by fat. The upper end of the vagina was then drawn into place and held by a stitch of catgut, and the lower border of skin sutured to the vulvar skin. As there was still slight oozing, a strip of rubber tissue was placed posteriorly between the vagina and the rectum and removed in twenty-four hours.

The patient had asked that the hypertrophied clitoris be removed, which was then done. In the healing, which was by primary intention over about two-thirds of the lines of incision, there was no evidence of too much cutting off of circulation, or too much tension as at the first operation, although there was marked edema anteriorly in the region of the amputated clitoris, making the necessary catheterization difficult. There was very slight infection, so slight that it did not interfere with the result.

The anatomic result is a vagina which admits two fingers, is three inches deep and is surrounded by soft tissues which give the impression of easy stretching

except in the midline, anteriorly. Perhaps if the vagina were rotated slightly on introduction, so that the line of sutures did not come in the median line, it might be better.

Whether the functional result is satisfactory has not yet been reported.

The operation has the disadvantage of a two-stage procedure with the intervening period.

The advantages of the operation are its simplicity and ease of performance; its range of applicability (any patient with normal thighs has ample skin for the two flaps); and the slight risk. There need be little hesitation on account of the danger, in contrast with the methods of intestinal resection. Whether it will generally prove satisfactory from the point of view of function, only further experience can determine.

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## SECONDARY ABDOMINAL PREGNANCY

By T. E. MENDENHALL, M.D., JOHNSTOWN, PA.

THE following case of secondary abdominal pregnancy presents four or five interesting features of sufficient infrequency to be worthy of report. The case is as follows:

Mrs. R., aged twenty-six, pregnant for the first time. General health had always been good. Well developed and nourished, weight 130 pounds.

Menstruation regular, every twenty-eight days, lasting four or five days and unaccompanied by pain. Last regular period November 12, 1927, normal. Slight irregular spotting during the next six weeks.

December 31 she was seized with a sharp pain in the left lower quadrant. Was in bed four days and felt all right again except for soreness of left side. During this time, until March 3, she had three other attacks of pain, not sufficient for a hypodermic and confining her to bed for only two days each time.

On March 3 she was admitted to the hospital and first came under my observation. At this time she had a tenderness in the left lower quadrant and in the left vaginal fornix. She had all the symptoms of pregnancy, with the uterus enlarged to the size of a small grapefruit. No mass could be made out in the culdesac. Satisfactory examination was extremely difficult on account of the nervousness of the patient and the small, tight vaginal tract. At this time her urine and blood pressure were normal. R.B.C. 4,000,000 and W.B.C. 11,000. This condition cleared up rapidly and in four days she was allowed to go home.

April 21 she was readmitted with severe pain in the right lower quadrant and with frequency of urination. This pain was so severe that although the urine was normal it would suggest the possibility of kidney colic. An x-ray examination was negative as to renal calculus. At this time her R.B.C. had dropped to 3,620,000 and her Hg. to 75 per cent. W.B.C. 8,200. Again the pain cleared up and she was allowed to go home.

Readmitted June 9 with pain in right lower quadrant, temperature normal, pulse 100. During this time the mass which was apparently the uterus had enlarged to



the level of the umbilicus. Fetal heart sounds distinctly heard in the left lower quadrant. At this time the R.B.C. was 3,320,000. Hg. 70 per cent. W.B.C. 9,000. During all of these attacks of pain, the patient was always relieved by high enema.

During the last week of July, fetal heart sounds not obtainable and fetal movements ceased. At this time the patient had moderate uterine contractions, passed a slight amount of colored blood and some pieces of tissue which proved to be decidua. This cleared up in twenty-four hours and the patient's general condition was improving. From this time on until August 22 careful measurements showed that the size of the mass was decreasing and the patient's general condition was improving. Her Hg. had gone up to 80 per cent, R.B.C. 4,290,000, W.B.C. 9,800, poly. 77 per cent, lymphocytes 20 per cent.

At this time an x-ray picture was taken in an effort to show overlapping sutures, to determine a dead baby which we strongly suspected. The picture showed a baby in a transverse position with the head in the lower right quadrant. No overlapping of the sutures could be determined. Repeated examination failed to elicit heart sounds or movements. At this time the patient was given nitrous oxide in order that a more satisfactory examination might be made. It was now determined that we were dealing with an abdominal pregnancy and a definite diagnosis of dead baby was made.

Inasmuch as the general condition of the patient was improving, and in the light of recent reported cases presenting the advisability of waiting on these cases for placental separation, we decided to wait.

On September 8 laparotomy was done. The abdomen was opened in the midline from the symphysis to two inches above the umbilicus. The uterus was found somewhat enlarged, dextroverted and crowded forward a little to the right of the bladder. The right tube and right round ligament were found tensely stretching across the mass which filled the posterior part of the pelvis. The placenta was found attached to the posterior part of the right broad ligament, the posterior surface of the uterus and to the ascending colon. The adhesions and attachments were easily separated with little hemorrhage. In an attempt to deliver the entire mass the sack was ruptured with the escape of considerable dark brown fluid. The left tube and ovary were removed with the mass. The left tube had apparently ruptured in the outer third. A part of the sack, 6 by 10 cm. was left in position, firmly adherent to the ascending colon. The abdomen was closed without drainage.

The fetus was a female 43 cm. long, weight 1375 gm. It had the following deformities: right club foot, both right and left elbows markedly flexed and unable to be straightened. The placenta weighed 560 gm. The baby occupied a transverse position, the head being in the left flank.

The following are the chief points of interest in this case: (1) Usual signs of pregnancy. (2) Definite symptoms of tubal rupture but not of sufficient severity to warrant laparotomy. (3) Continued uniform enlargement of the uterus during the first three months. (4) Although this was a left tubal pregnancy, the major portion of the placental attachment was in the region of the right posterior surface of the uterus, the right broad ligament and the ascending colon. (5) At the time the baby perished, definite labor symptoms started and the decidua was passed. (6) During the interval between the death of the baby and the operation, the placenta had largely detached itself and was easily removed without hemorrhage.

MATERNITY HOSPITAL.

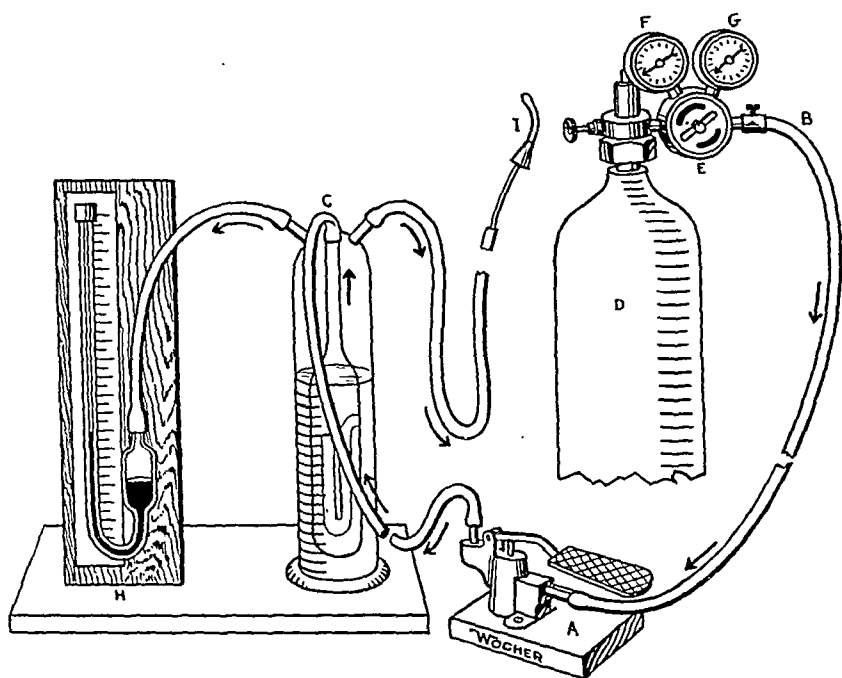
## A NEW GAS CONTROL VALVE FOR THE RUBIN TEST

BY GILBERT MOMBACH, M.D., CINCINNATI, OHIO

*Attending Obstetrician, Jewish Hospital.*

THE usual method for controlling the gas which is led into the uterus during a Rubin test is by means of a small needle valve which when closed permits the gas to flow into the cannula, and which when open allows the gas to escape into the atmosphere. This valve is identical with the one used on the bulb of a blood pressure outfit. Such a valve requires really two hands to manipulate and often is responsible for minute leaks.

The author conceived the idea of placing a foot control valve (*A*) in the main gas line between the needle valve (*B*) on the tank and the inlet of the siphon flow meter (*C*). This valve is mounted on a heavy base which is placed at the foot of the examining table. The hose to and from this valve is of sufficient length to permit the valve to be placed at some distance from the tank. This valve is operated by a foot pedal which operates a spring controlled plunger. The removal



of the foot from the valve immediately shuts off the gas. Where a recording kymograph is used in conjunction with the Rubin outfit this valve has been found ideal. In those cases where it is desired to open tubes which are closed, such a valve is of inestimable value, as the gas can be instantaneously shut off, whereas with a hand operated valve an excessive pressure may be produced because of the difficulty of manipulating the hand valve. The advantages to be derived from the foot control valve are:

1. The Rubin outfit and tanks can be placed on a shelf or in a corner quite some distance from the examining table.

2. The operator has both hands free and can keep them sterile during the test.
3. Instantaneous control of the flow of gas.
4. The avoidance of excessive pressures due to the inability to quickly release the hand controlled valve.
5. Minute leaks due to the hand controlled valve are avoided.
6. The valve is portable and it can be readily taken away from the examining table when the test is finished.

The author uses a kymograph to record the fluctuations of the manometer. He uses in conjunction with the above described foot valve a remote control switch which starts the electric driven kymograph. He is able at all times to do the entire test without the aid of an assistant.

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v. Varo, B.: Extirpation of Ovarian Tumors During Pregnancy. *Monatschr. f. Geburtsh. u. Gynäk.* 74: 28, 1926.

During the last twelve years among 22,750 obstetric patients in the first woman's clinic of Budapest, 30 cases were found complicated by ovarian cysts (0.13 per cent). During the same period of time, 695 women were admitted with a diagnosis of ovarian cyst and 30 of these women (4.1 per cent) were pregnant at the time of admission.

All but one of the 30 patients in whom an ovarian cyst complicated pregnancy were operated upon during the first half of pregnancy. Not one of these patients knew they had an ovarian cyst before pregnancy. In 4 patients both ovaries were removed during the first four months of pregnancy and in none was the gestation interrupted. Of the 30 cysts, 3 were dermoids, 3 were papillary carcinomas, and the remainder were simple serous cysts. In 3 cases torsion was present.

All the cysts were removed by laparotomy and all the patients received novatropin and papaverin for four or five days after operation to reduce the irritability of the uterus. In 90 per cent of the cases, pregnancy continued in spite of the operation.

The author believes that in every instance where an ovarian cyst is found during pregnancy, the cyst should be removed because it might cause a miscarriage or serious complications during labor and the puerperium. The danger of operation is not greater during pregnancy than it is at any other time. There were no deaths in this series. An operation for cyst complicating pregnancy should not be performed at a time when the menses would have appeared, were the patient not pregnant, because the uterus is most irritable at this time.

J. P. GREENHILL.

# Society Transactions

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## NEW YORK OBSTETRICAL SOCIETY

MEETING OF FEBRUARY 12, 1929

### DR. A. C. BECK reported a case of **Spontaneous Rupture of Uterus in a Multipara With Specimen Showing Arrangement of Uterine Musculature.**

Mrs. H. P., Italian, was admitted to the prenatal clinic of the Long Island College Hospital October 31, 1927, in the fourth month of her ninth pregnancy.

Six of the previous pregnancies had terminated in the spontaneous delivery of living infants at term, twenty-one, seventeen, fifteen, eight, six, and two and one-half years before admission. Nine years ago she gave birth to an eight months' dead fetus and subsequently aborted at two and one-half months. During the eighth pregnancy she also was under the care of the prenatal clinic and received salvarsan and mercury on the recommendation of her family physician who had treated her husband for syphilis and believed that several of the older children were syphilitic. Prior to and following treatment her Wassermann test was negative. She entered the hospital June 23, 1925, and was delivered of a well-developed living child which was 52.5 cm. long and weighed 4300 gm. Labor was spontaneous and lasted four hours and thirty minutes. The history of this, the only previous labor conducted by our service, was quite normal, and following an uneventful puerperium, the patient and her child were discharged on the fourteenth day after confinement.

During the last five months of the ninth pregnancy she again was under the supervision of our prenatal clinic. Physical examination revealed no abnormalities. Pelvic measurements were as follows: interspinous diameter 29 cm., intercrystal 31, introchanteric 33, external conjugate 20, diagonal conjugate not reached, biischial 9 cm. The Wassermann test was repeatedly negative and no other findings of syphilis could be discovered. As several of her children were being treated for syphilis in the syphilitic clinic, one course of salvarsan and mercury was given the patient during the last trimester.

Labor began at 10 P.M. on April 12, 1928. At 11:30 P.M. examination revealed a large child presenting as an L.O.A. position; the fetal heart was good, the cervix was 3 to 4 cm. in diameter; membranes were intact, the head was at level of the ischial spines; pains were strong and recurring at two- to three-minute intervals. At 11:45 P.M. the cervix was 5 to 6 cm. in diameter and severe pains were coming every two minutes. Preparations for delivery were made at once. At 11:55 P.M., following a very severe contraction, the pains ceased and the patient became pale and pulseless. Blood pressure was too low to be determined. Abdominal palpation showed the small parts to be closer to the abdominal wall than previously noted. The back of the child was easily made out on the left and the uterus could be definitely outlined on the right side near the umbilicus (Fig. 1). Rectal examination showed the head at the level of the ischial spines and apparently through the cervix. After gently pushing the presenting part upward a slight trickle of blood was observed to come from the vagina. A diagnosis of rupture of the uterus was made, and a quarter of a grain of morphine was immediately given.

At 12:20 A.M. a second dose of morphine was given in place of an anesthetic and although the patient was pulseless, the abdomen was opened in the midline below the umbilicus. The peritoneal cavity was filled with bright red blood and all but the face of the child was found to be outside of the uterus. After removing the child an extensive rupture of the uterus and left broad ligament was observed. The tear extended from the external os to a point almost on a level with the attachment of the left round ligament and included the uterine artery, the proximal end of which had retracted beyond view (Fig. 2). The left ovarian vessels were clamped with the left infundibulopelvic ligament and after stripping the bladder from the anterior wall of the uterus the uterine and ovarian vessels on the right side were similarly handled. The entire uterus was quickly

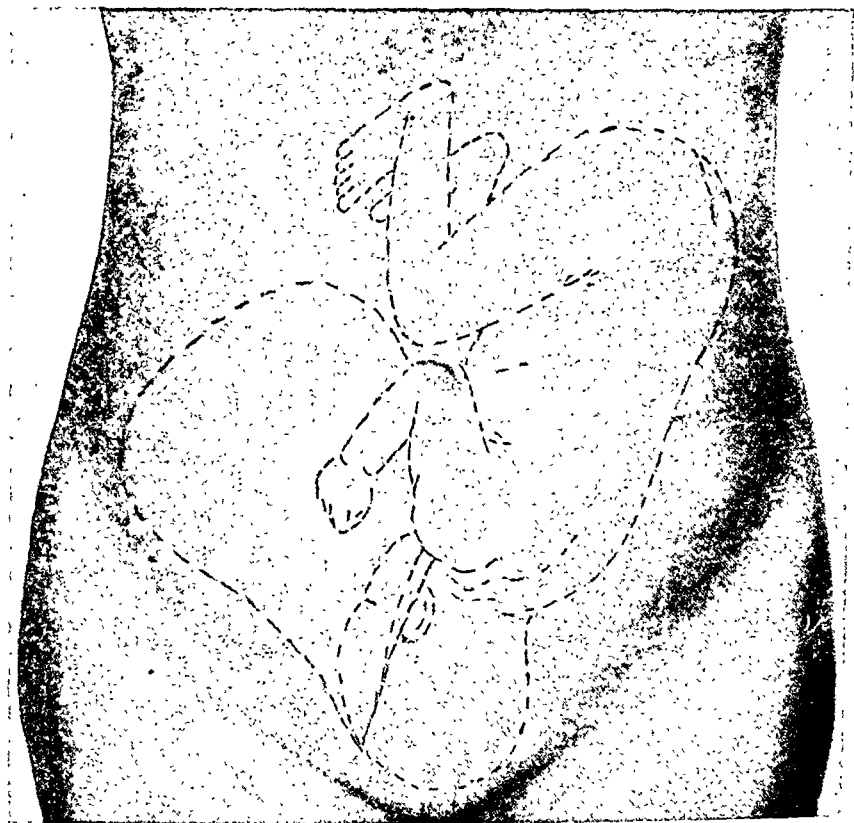


Fig. 1.—Findings on abdominal palpation after rupture of the uterus.

removed and the remaining bleeding points were caught by forceps. Additional hemostasis was obtained by the use of three wide gauze packs. All clamps (16 in number) were left in place and protruded through the lower angle of the abdominal wound. The remainder of the incision was closed with two interrupted silkworm gut sutures. Immediately after the vessels were clamped 1000 c.c. of saline were given intravenously and a transfusion of 500 c.c. of blood was started. Before the patient was taken from the operating room her pulse was perceptible but could not be counted. The usual postoperative routine was carried out and at 4:15 A.M. her pulse was 150.

The clamps were loosened on the third day and removed twenty-four hours later without any evidence of hemorrhage. At the end of one week the removal of the gauze drains was started and a small amount was removed daily for ten

days. The temperature was elevated for forty-one days. Throughout the first month after operation it reached a height of  $103^{\circ}$  to  $104^{\circ}$  daily. During this time the pulse varied between 140 and 120. After a protracted convalescence the patient was discharged from the hospital on the seventeenth of June, 1928. Examination at this time showed fair healing of abdominal incision, except at its lower angle where a sinus about 1 cm. in diameter was still draining. Vaginal vault was high and healed. On the left side a small insensitive mass could be felt. On the twenty-third of December, 1928, she was examined in the follow-up clinic where the following findings were noted: Fair abdominal wound, poorly healed in its lower angle, weak spot at drainage point, good pelvic floor. High well-healed vaginal vault. No parametrial tenderness or mass.

The child was well developed, 54 cm. long and weighed 4200 gm. Uterus was 24 by  $12\frac{1}{2}$  by  $9\frac{1}{2}$  cm. Left lateral aspect presented a tear extending from the level of the implantation of the round ligament to the external os. Retracted

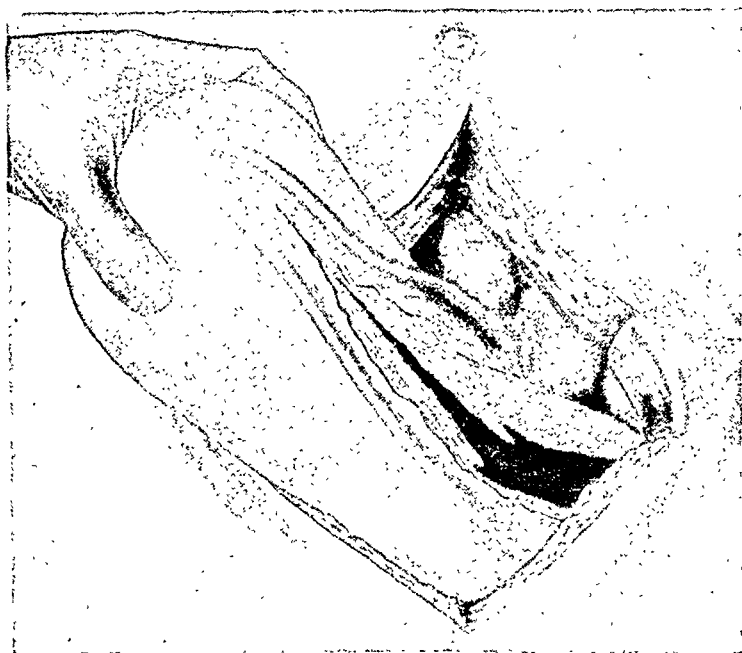


Fig. 2.—Appearance of rupture of uterus and broad ligament after child was removed.

wound measured 15 cm. by 6 cm. Muscle at site of tear presented a marked interstitial hemorrhage. Remainder of organ was normal. Placenta and membranes in situ. Former was implanted on posterior body and fundal walls and extended to site of tear. Myometrium remote from the site of trauma presented no departure from the normal and measured  $2\frac{1}{2}$  cm. in thickness. Section made at site of tear showed microscopically the following: Membranes frequently revealed. Decidua thin but well shown. Capillaries markedly engorged. Myometrium hyperplastic and hypertrophied as in pregnancy. No evidence of scar formation. Tubes and ovaries normal. Corpus luteum of pregnancy present in right ovary.

*Diagnosis.*—Physiologic changes of pregnancy in uterus with uterine rupture. Tubes and ovaries normal. Several months later the specimen was again studied. At the site of the rupture the myometrium had retracted irregularly and revealed the peculiar interlacing of the muscle bundles shown in Fig. 3. These will be carefully studied in the hope that some accurate observations as to the muscular arrangement of the uterus may be made.

*Comment.*—The points of interest in this case are:

1. Spontaneous rupture of the uterus in a multipara who had previously given birth to 6 full-term infants without any difficulty.
2. Even though the tear in the uterus and broad ligament severed some of the large vessels, the patient did not die before laparotomy could be done.

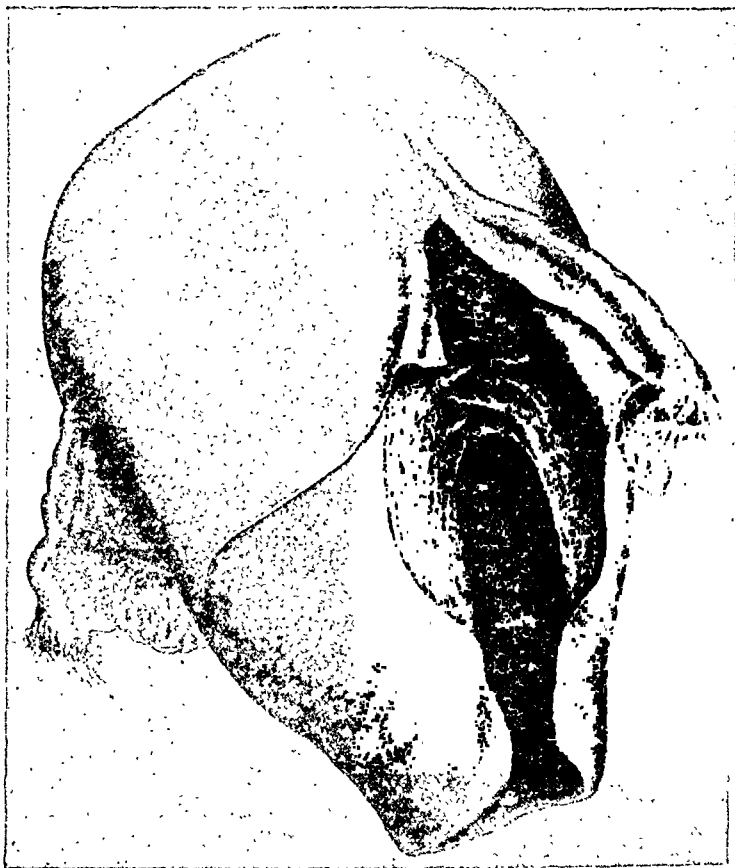


Fig. 3.—Uterus removed at operation, showing rupture and peculiar interlacing of uterine musculature.

3. Clamps may safely be left on vessels to be removed several days later when the patient's condition will not permit the use of a more finished technic.

4. The appearance of the tear in the uterus after fixation may give us a clue as to the arrangement of the uterine muscle fibers.

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DR. E. M. HAWKS (by invitation) presented a paper entitled **Maternal Mortality in 582 Abdominal Cesarean Sections**. (For original article see page 393.)

#### DISCUSSION

DR. G. L. BRODHEAD had seen three cases of uterine rupture. The first was in the outdoor service of Post-Graduate Hospital in 1909, a para vi, thirty-seven years of age. She had had four normal labors and one abortion followed by a curettage. The curettage immediately preceded the labor during which the uterus ruptured.

Labor came on at term and after some hours the woman complained of a very severe pain in the left side and told the doctor "the baby was born." He made a vaginal examination and found the cervix was about three fingers' dilated, just as it had been at the time of the last examination, but the patient's condition became steadily worse and she was brought into the hospital. The patient's condition resembled a concealed accidental hemorrhage, the uterus being very tender and in tonic contraction. As the head was presenting in the pelvis and the child was dead, craniotomy was done and a small fetus very easily removed. The fundus was at the level of the navel and the placenta was expressed easily. On passing the hand up into the uterus a rupture into the peritoneal cavity on the left side was found. An immediate laparotomy was done. As the tear was fairly clean-cut and there was very little bleeding, the uterus was sewed up and the patient made an uneventful recovery. The cause of this rupture may perhaps be due to too vigorous curettage after the abortion which preceded the labor.

The second case was also in the service at Post-Graduate Hospital in May, 1912. In this instance the patient was thirty-three years of age; she had had six normal labors and three abortions. The membranes ruptured five days before this labor. She was seen at 2:00 o'clock in the morning. The cervix was a finger and a half dilated. At 8:45 A.M. the patient went into shock after a very severe pain, and then all the pain ceased. Her condition became very serious and before the ambulance could reach the home, the woman died.

The third case was at the Harlem Hospital. This patient was thirty-five years of age, and had had six normal labors. The woman was eight months pregnant, and had had a premature rupture of the membranes. After twenty-four hours of intermittent pain she was brought into the hospital. There was a history of no fetal movements for a week. There was moderate dyspnea and slight cyanosis, a pulse of 110, and no fetal heart, apparently a breech presentation. The cervix was closed. A No. 4 bag was inserted at 10 P.M., and the next day as conditions had not changed the abdomen was opened. Floating among the intestines was a large anencephalic monster. The uterus showed a tear down the anterior wall about five inches in length, the uterus was well contracted, but it was removed by hysterectomy. The patient made a good recovery.

DR. A. H. MORSE had seen a case of ruptured uterus in a multipara, who was believed to be in the first stage of labor. She had a sudden attack of pain and was taken to the delivery room with the expectation that the head would appear on the perineum. Upon examination it was found that there was a rupture of the uterus. A hysterectomy was done immediately. The tear in this case was much like the one which was shown in Dr. Beck's specimen, namely, in the left hand side, extending from about the region of the broad ligament down into the cervix. There was no tear of the uterine artery. The operation was carried out without any great difficulty and the patient made a good recovery. He could find no evidence of a weakness in the uterine wall on that side, but there was this history: that when she was about three months pregnant, she went to a physician who attempted to do an abortion, apparently by curettage. The attempt was not successful and the patient went on. She also had a laparotomy because a physician had discovered a tumor not diagnosed as a pregnant uterus, but it seems the conditions in the pelvis were found perfectly normal.

DR. J. O. POLAK said he had had no experience with the Latzko operation, but had with the so-called exclusion operation, although the technic which he employed had been that known as the Veit-Fromme. The only criticism of the operation is the tardy involution of the uterus when it is repaired. Dr. Polak



now had five of these patients under observation with uteri that are well above the umbilicus, all complaining of metrorrhagia.

The other important point brought out is the reduction in the incidence of peritonitis. Dr. Polak believed that it was not due to the spill, because the spill can, with proper technic, be absolutely prevented, but the fact that the primary infection was an endometritis which extended through the suture line and infected the peritoneum, just as our abdominal wounds are infected along the suture line in the through-and-through suture. These cases have been minimized by the adoption of some form of flap operation, whether it be the Beck, Kroenig or DeLee type.

The third important point brought out was the question of local anesthesia. Dr. Polak believed that the more we develop its use, the more we are going to obviate certain things. First of all, we can control the convalescence much better, we can control the intestinal soiling much better and, with local anesthesia, which can be used with very little difficulty if one will only take the trouble to use it, neglected cases can be saved. Preeclampsias who are bad risk cases, are particularly suited to it.

The final results with so many men operating, are encouraging. Where there is only one man operating, he will get a very low mortality for several hundred cases, but in clinics where there are a large number of men operating there is bound to be a higher mortality.

Dr. A. C. BECK said that this paper was a triumph for the low operation. As we see various analyses from different parts, we are learning that some type of the low operation in any kind of a case that can stand operation, is the preferable type. For instance, Gordon showed that the mortality of the classical operation when done under elective circumstances, that is, on women who had not been in labor, or were just in labor, where the membranes were intact and no vaginal examinations had been made (the ideal case for section), was considerable, and that it was due to peritonitis.

Now, the low procedure, no matter how it is done, offers considerable protection against peritonitis, and therefore the classical procedure should be limited to those cases where the matter of time is an important consideration.

DR. S. J. SCADRON said that the cases of maternal deaths from tuberculous meningitis referred to by Dr. Hawks, were two unfortunate cases, yet interesting. They were unfortunate from the standpoint of fatality, but very interesting from the standpoint of diagnosis and their coincidence.

Both patients were sectioned within twenty-four hours. Both received spinal anesthesia. Both died from the same malady, one living three weeks postoperative and the other four weeks. There was no contraindication to general anesthesia. Spinal anesthesia was used because he had employed it with very good results and without untoward effects on the mother or the child.

Both patients were sectioned for contracted pelves. One was a primipara and the other was a repeated section.

The previous history of the first patient was interesting because she had had a tuberculous arthritis for seven years which had been treated. He pronounced her cured three years prior to her conception. The second patient gave no previous history of tuberculosis.

The first case was in labor for twelve hours previous to section. The second case was operated upon soon after her admission to the hospital, in labor.

The subjective symptoms postoperatively were practically uniform. For the first three days the patients complained of slight abdominal pain, and distention,

which was relieved on the third day, following an enema. On the third day post-operatively, the patients complained of headache, drowsiness, insomnia, and slept only at short intervals. They began to improve on the third or fourth day, but about the twelfth day postpartum they developed symptoms of meningismus, rigidity of the neck, headache, hiccough, photophobia, and vomiting.

The temperature of these patients was uniform. For the first week it was between 99.2 and 102.6; the second week between 98.6 and 101.6; the third week, in the first case, it was as high as 103, and in the second case, which lived one week longer, it ran exactly the same course.

A very interesting point was that the pulse never ran higher than 100. It usually ran between 60 and 88.

They had primary union in their wounds and were practically normal from an obstetric and surgical standpoint.

When the patients developed symptoms of meningismus, Dr. Scadron attributed this to the spinal anesthesia, and knowing that sometimes an ordinary spinal puncture causes meningismus, he then deemed it advisable to consult with a neurologist who confirmed the diagnosis.

DR. I. C. RUBIN said that Dr. Polak's remarks about the low mortality rate at the Nursery and Child's Hospital may be partly explained by the fact that the hospital is chiefly an obstetric hospital; that there is a minimum amount of gynecology done in proportion to obstetrics; and that the gynecologic operations that are done there are done almost exclusively on clean cases. There are very few infections postoperatively. Now, that perhaps is a fact that may be overlooked in accounting for the relatively low mortality, a mortality which is particularly low as regards peritonitis and sepsis. Sepsis was almost absent with the exception of one case out of that whole series, and peritonitis is getting more rare.

DR. HAWKS (closing) said in reply to Dr. Polak's question as to high fixation of the uterus following the operation of peritoneal exclusion that in the one case with the uterus fixed high, so that the fundus was at the level of the umbilicus, the patient had no complaints.

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## NEW YORK OBSTETRICAL SOCIETY

MEETING OF MARCH 12, 1929

DR. SAMUEL H. GEIST read a paper entitled **The Morphology of Normal Menstrual Blood and Its Diagnostic Value.** (For original article see page 321.)

DR. T. E. LAVELL (by invitation) presented **The Diagnosis of Ectopic Gestation.** (For original article see page 379.)

### DISCUSSION

DR. HOWARD C. TAYLOR said with reference to the large number of cases operated upon the first day when patients appeared in the hospital, that this was unusual in his service and that the actual number of cases operated upon immediately is a much smaller percentage than Dr. Lavell had shown. It is agreed that when a positive diagnosis of ectopic pregnancy is made there is nothing to be gained by waiting. On the other hand, there are a large number of cases where

we have the possibility of pregnancy in mind, but recognize also that it might not be ectopic pregnancy but an acute inflammatory condition and there certainly is no harm in waiting for a considerable length of time. Dr. Taylor's custom is not to hurry the operation for ectopic pregnancy unless it is a shock case where there is a possibility of bleeding still going on. The percentage of error in diagnosis is interesting, too, and probably is about the same as others have. It would be interesting if we could know the number of cases operated upon with a diagnosis of ectopic and something else was found.

DR. S. H. GEIST asked whether there were any data on the frequency with which uterine casts were expelled and when in relation to the operation or to the initial bleeding, these casts were obtained.

A second question is one relative to the nonbleeding cases. In what proportion of those cases were the ectopics presumably alive? That is, a perfectly viable fetus or nonrupture, or abortion in the tube, and in what proportion of those nonbleeding cases pain was absent.

DR. H. C. COE was sure that in working at Bellevue Hospital and elsewhere he had come across cases of true tubal abortion which were cured without operation, and also cases of apparently tubal abortion, which suggested to his mind the old question of tubal menstruation. It may be rather an old-fashioned idea, but he believes that under certain conditions it is possible for the tubes to extrude menstrual blood from the distal ends. Such cases are not ectopics, as shown by examination of the blood and of the tubes. He sees no reason why we should not have a tubal menstruation which simulates tubal abortion.

Of course, there is no question about operating immediately on patients where the diagnosis has clearly been made, but there are so many different kinds of ectopics and so many different conditions under which we see the patient (at least we used to do so at Bellevue Hospital), that it is difficult to lay down any hard and fast rule with regard to operation.

DR. WALTER T. DANNREUTHER said that one frequent symptom which was not mentioned, is the sensitiveness of the cervix on manipulation. In his experience, this was found more often than exquisite sensitiveness of the mass itself.

It has always seemed to him that the symptom-complex in a particular case of ectopic pregnancy can well be correlated with our conception of the underlying pathology. For example, in the early cases with slight hemorrhage and complete extrusion of the gestation sac into the culdesac, we expect the symptomatology to be meager. Patients suffering from small repeated hemorrhages more often conform with the classic textbook clinical picture, and often complain of soreness in the lower abdomen between acute attacks of pain. In case of sudden rupture of the tube, the patient is precipitated into a stage of shock, the so-called tragic state of the disease.

The treatment of the several groups of cases is well predicated on the symptomatology and the type of pathology presented. Within the past two months a patient under observation in the ward for purposes of differential diagnosis manifested signs of mild shock while being given an enema. The change in her condition was recognized, and the patient was operated upon immediately. Laparotomy revealed a tubal gestation sac which previously probably had not existed. Two weeks later Dr. Dannreuther operated upon another patient, having made a definite diagnosis of ectopic pregnancy after careful study, and found no pregnancy at all. All patients presenting symptoms which arouse suspicion of a tubal pregnancy should be confined to the hospital under close observation until the differential diagnosis has been established.

DR. LAVELL (closing) said that the paper was purposely limited to the features which had a bearing on diagnosis.

The operative death rate was 2.68 per cent and is influenced a good deal by the type of case. Bellevue has a very active ambulance service and receives many cases in shock. Many have died on the way to the hospital, or within a few minutes after admission. The policy is to operate as soon as possible after a diagnosis is made, although there is a great advantage in some preliminary rest and treatment for the more serious cases.

In reply to Dr. Geist's question, he found that decidual casts are very seldom reported by the patient and seldom seen in the hospital. In regard to the viability of the fetus, it is to be remembered that these are practically all early cases, and practically all ruptured or aborted. The full-term or viable ectopics are taken care of on the Obstetric Service.

A past history of severe pelvic infection was very, very rare. Often there had been symptoms suggestive of mild chronic infection. However, there were very few that had previously been on our own ward for infection. Their impression in this series is that the type of infection that predisposes to ectopic is very mild. Probably if it is severe, it causes sterility, or a hysterectomy or salpingectomy is done following the infection.

In answer to Dr. Kosmak, in no case was a salpingostomy done for unruptured ectopic. Most of these cases had partial or complete salpingectomy.

Relative to Dr. Ward's discussion: they did not make daily blood counts with the idea of differentiating hemorrhage from infection. If there is a leucocytosis, he would rather rely on other signs to differentiate between acute hemorrhage or infection. The sedimentation test is more reliable to indicate not only the presence but the degree of infection, but he felt that the red blood count, hemoglobin estimation, blood pressure reading, and symptoms of the patient give us better information about hemorrhage than the white blood count.

Dr. Lavell agreed with Dr. Grad on the value of colpotomy. Not only is it necessary to clear up a doubtful diagnosis, but it is a measure of safety to avoid doing a laparotomy on a dangerous type of acute infection. However, from the standpoint of abstract diagnosis, it is not advisable to depend on any method of exploratory operation.

Dr. Lavell had not practiced the method of retransfusion mentioned by Dr. Grad. Some years ago the custom was to fill the abdomen with saline in exsanguinated cases, but now we try to give a transfusion during the operation or shortly after. If blood cannot be obtained soon enough for this purpose, we give them a saline infusion during the operation, and practically all have a hypodermoclysis and Harris drip as soon as they reach the recovery room.

In reply to Dr. Dannreuther, he said he found it very hard to tabulate the number of cases that had a tender cervix, partly because the examiner so often failed to mention it. His own opinion was that a cervix which is painful on motion is suggestive, but not characteristic of ectopic and is found much more frequently in acute or subacute inflammation. If these can be ruled out, the sign becomes increasingly significant.

He was not able to find many cases where the examiner described a pulsating mass and believed that this also is more common in inflammatory conditions than in ectopics. There seems to me no reason why a ruptured or aborted ectopic should have an expansile pulsation, although any mass may transmit a pulsation from the large pelvic blood vessels.

Neither did he consider a soft, or blue, or patulous cervix as really characteristic of ectopic. In fact, these were not mentioned very many times in this series.

# Department of Reviews and Abstracts

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CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

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## Selected Abstracts

### Pregnancy and Disease

Ratner, Jackson and Gruehl: Transmission of Protein Sensitiveness from Mother to Offspring. *J. Immunol.* 14: 249, 267, 275, 291, and 303, 1927.

In a series of five studies the authors offer an explanation for the underlying basis of allergic reaction at times occurring in early infancy as a result of contact with a food for the first time.

There is clinical evidence that sensitization may be transferred from mother to offspring. The conception of earlier investigators was that the placenta, irrespective of animal species, was impermeable to protein and did not permit the passage of maternal antibodies except it was injured either through disease or heterologous proteins such as horse serum antitoxin often employed in these experiments. They therefore contended that placental transmission of antibodies was a pathologic and not a physiologic process. From their own study the writers arrive, however, at the conclusion, that this interchange is a physiologic one and is brought about largely by means of mechanical filtration. This placental permeability occurs consistently in the human being with such substances as protein sensitizing antibodies, antitoxins, agglutinins, precipitins, bacteriolysins, chemical blood constituents, etc. The theory of placental transmission of immune bodies as a result of placental injury has become untenable. Evident differences in this respect between the human and certain animals shown in experiments are seemingly plausibly explained by the fact that in the human placenta the maternal blood is separated from the fetal by a single cell layer, whereas e.g., in the case of the ruminants the placenta consists of three cell layers.

The second paper of the series deals with the possible transference of such substances through the colostrum. While an essential medium for the transmission of immunity from a mother ruminant to her newborn (goats, and cattle), colostrum plays only a negligible rôle in this respect in rodentia (guinea pigs and rabbits) and in the human species. There is no work recorded in literature on the transmission of protein hypersensitivity through the colostrum.

Turning next to the rôle of milk played in this respect these authors state that there are certain clinical indications which have suggested the possibility that the breast milk of the mother might transmit foreign proteins and thus produce nutritional and allergic disturbances in the nursing. In their own experiments on guinea pigs they were unable to reproduce such passage of proteins. They conclude that for the present this question must be answered in the negative. An analysis of literature dealing with the passage of immune and other bodies through breast milk reveals a mass of experiments that at first hand seem contradictory. An evaluation of succeeding experiments, however, demonstrates quite clearly that many antibodies do enter the milk of nursing mothers although always in lessened amounts but that in only a few instances do these milk-borne antibodies gain

entrance into the suckling's body and then persist there only for an extremely short time. With the human being, the overwhelming evidence is definitely against the passage of agglutinins into the nursing through the milk.

Passive sensitization of the offspring is clearly proved by their experiments with mother guinea pigs made sensitive to horse serum before conception. The offspring will be born sensitive to this same substance. This phenomenon is due solely to placental transfer and is in no wise hereditary. This state of hypersensitiveness is transmitted to successive litters. It is a passive state and disappears later.

As shown in the last paper of the series, the fetus in utero can also be actively sensitized. The actual presence of protein traversing the placenta and entering the fetal circulation does not necessarily mean that the fetus has become sensitized to the protein. This is fully shown in the protocols of their experiments. It proved to them a very difficult task to actively sensitize the fetus in utero as compared with the simple task of demonstrating the passive transfer of antibodies.

They conclude that active and passive sensitization of the fetus offers a probable explanation for the occurrence of allergic manifestations in infants that come in contact with a protein for the first time.

HUGO EHRENFEST.

Sano, J: The Resistance of the Gravid Animal to Various Kinds of Bacillus Toxins. Japanese J. Obst. & Gynec. 10: 17, 1927.

It is recognized that the gravid animal has a weakened resistance to bacillus toxins. This decrease in the resistance might be due to special conditions accompanying pregnancy, such as abortion or the incident blood loss, or to marked anatomic changes in the uterus. But even in the pregnant animal, not aborting and without recognizable uterine change, there exists this diminution in resistance. Thus it must be inferred that the fundamental cause is supplied by pregnancy itself.

Whether this reduced resistance is connected with the vitality of the organism during pregnancy, is a difficult problem to settle, but the results of the author's experiments offer a clue. It was noted in the first series of experiments that when intoxication was mild the gravid animals had fewer symptoms than the nongravid animals. In the second series of experiments it was seen that the hypertrophy and hyperplasia of the reticuloendothelial cells was frequently and especially marked in the gravid animals. In the third series of experiments it was seen that in the case of weak intoxication leucocytosis was more marked in the gravid than in the nongravid. These facts indicate an increase of vitality in the gravid animals. In the majority of cases, on the other hand, their resistance was inferior to that of the nongravid animals. It may be inferred that at the time of pregnancy there are increasing burdens imposed on the maternal body, such as the nutrition of the fetus or the equilibrium of metabolism, and thus all the organs are in a state of stimulated energy. The constant stimulation, however, leads to insufficiency in reserve energy, so that once intoxication is heightened or prolonged, the whole organism is apt to yield to the invasion of the toxin. In short, during pregnancy much less surplus energy is available than in the nonpregnant state, and consequently the invasion of toxins is rendered much easier.

J. P. GREENHILL.

Goldschmidt, H: The Development of the Newborn During Sickness of the Mother. Klin. Wchnschr. 6: 207, 1927.

Since nothing can completely replace mother's milk as the ideal nourishment for the newborn, the author investigated the results obtained by keeping newborn babies at the breast in spite of various types of infectious diseases of the mother

which have usually been looked upon as contraindications to nursing. The only precautions necessary are first that the maternal milk shall not be infected or contaminated and secondly that in infectious diseases of the respiratory tract, the mother's mouth and nose shall be masked during nursing.

In the grippal infections, 91 per cent of the babies had only mother's milk and 50 per cent of these passed their birth weight in less than twenty days. Pneumonia decreases the milk supply of the mother to a considerable extent, only 37 per cent having sufficient breast milk. Of these babies 72 per cent regained birth weight in twenty days. The only justification for stopping nursing in cases of pneumonia, where the milk supply is sufficient, is extreme weakness of the mother.

Of the 32 cases of mastitis studied, 57 per cent thrived on breast milk alone. The author has never seen any harmful effect from allowing a baby to continue nursing in these cases. The only contraindication is pus contamination of the milk or an erysipeloid infection involving the nipple.

There were 65 cases suffering from endometritis, parametritis, thrombosis or thrombophlebitis but 42 nursed their babies completely. These conditions do seem to have a harmful effect upon the babies in that only a small percentage regained their birth weights.

Those mothers who were suffering from gonorrheal infections or from syphilis were allowed to nurse and all of their babies passed their birth weights during the first three weeks. Breast feeding is especially valuable in cases under anti-syphilitic treatment. In eclampsia the author considers it well to allow several days to elapse after an attack before putting the baby at the breast.

RALPH A. REIS.

**Pineda, E. V.:** The Presence of *Mycobacterium Leprae* in the Placenta and Umbilical Cord. *J. Philippine Islands M. A.* 8: 67, 1928.

Of 104 placentas examined, 57 (53 per cent) were found positive. In 25 cases (24 per cent) the organism was also found in the cord blood. In only one case was the organism found in the cord and not in the placenta. Histologic examination of placenta and cord showed no pathologic changes attributable to leprosy.

The bacillus of leprosy reaches the fetus in a considerable proportion of cases, although in the majority it is probably finally overcome. Intrauterine infection in leprosy should be considered in some cases, particularly when the disease develops in early infancy.

C. O. MALAND.

**Hitzanides, E.:** The Influence of Dengue Fever on Pregnancy and Labor. *Bull. Soc. d'Obst. et de gynéc.* 18: 133, 1929.

When dengue is contracted by a pregnant woman in the first half of pregnancy, abortion may result but when the disease is acquired later in pregnancy, the gestation remains unimpaired. Abortions were not determined by the severity in the cases seen by the author for in many severe cases the pregnancy continued uninterrupted whereas in some mild cases, abortions occurred. Dengue produced hemorrhages in pregnant women which lasted from a few days to a few weeks. When an abortion occurred it usually did not take place at the height of the attack but later during a remission which varied from several days to a few weeks.

In the observed cases, the duration of labor was normal. In some cases large clots were found adherent to the maternal surface of the placenta and sometimes uterine inertia was present. All the cases but one had normal involution of the uterus. When dengue is contracted for the first time during the puerperium, it

may be difficult to differentiate it from puerperal sepsis. However, in dengue, bradycardia and leucopenia are constant findings. In two cases the newborn babies had dengue.

J. P. GREENHILL.

**Rhenter and Savoye: Nine Cases of Typhoid Fever During the Puerperal State.**  
Bull. Soc. d'obst. et de gynec. 18: 242, 1929.

In an epidemic of typhoid fever in a suburb of Lyons, nine cases occurred in women who were pregnant or had recently been delivered. Two were serious cases and seven were mild. Pregnancy was interrupted only once among seven pregnant women. Two children died during pregnancy and both mothers of these children likewise died. Hence fetal mortality is evidently associated with severity of the disease. No connection was found between the duration of pregnancy and the frequency of interruption of pregnancy. All the children born alive were in good condition and of normal weight.

J. P. GREENHILL.

**Phillip: The Latest Knowledge and Treatment of Syphilis in Mother and Child.**  
Ztschr. f. Geburtsh. u. Gynäk. 93: 442, 1928.

In Berlin about 6 per cent of the obstetric clinical material is syphilitic. The infection of the fetus occurs through the placenta at about the fourth or fifth month. Ninety-five out of 100 untreated syphilitic mothers will bear syphilitic children. When the mother is treated before pregnancy, 78 per cent of children will be infected. If the mother is treated during pregnancy only 22 per cent of the children will have syphilis.

The diagnosis is difficult because the pregnancy may cause a positive Wassermann reaction. The author uses three methods on each patient, the Wassermann, Meinicke and Sacks-Klopstock, and if two or all three are positive the diagnosis most certainly is syphilis.

The serologic reaction in newborn syphilitic children is negative in 80 per cent. It does not become positive until some time later. The diagnosis may be more easily made by examining some of the tissue fluid, taken from the cord near the navel, by the dark-field method. A negative result does not mean a healthy child. A further help is the x-ray appearance of the child's bones if they show a syphilitic osteochondrosis.

It is of the greatest importance to treat the syphilitic mother early in pregnancy and, if possible, before the fetus is infected.

FRANK A. PEMBERTON.

**Almkvist, J.: Has the Impossibility of Direct Transmission of Syphilis from Father to Fetus Been Proved?** Wien. klin. Wchnschr. 42: 97, 1929.

Matzenauer in his article on "The Inheritance of Syphilis," in 1903, made the statement that "a transmission of the disease directly from father to child has not been proved." Almkvist maintains that "not proved" does not mean "impossible," and deplores the tendency of the profession to accept the statement as dogma, making no allowance for exceptions. He cites 67 cases of women who have borne syphilitic children, 28 of whom knew nothing of a syphilitic infection. Of these, 5, or about 7.5 per cent of all the cases, showed no signs of the disease, clinically or serologically, on repeated examinations. One of the 5 has been studied for fourteen years and has had 36 examinations both clinical and serologic during this period, with entirely negative results. Ten years after bearing a syphilitic



child, the patient, by a second marriage, bore a normal healthy child which has never shown evidence of syphilis. At no time had the patient had antisyphilitic treatment. The author points out that the above case must lead us to entertain the possibility of direct transmission from father to child, and pleads that indiscriminate antisyphilitic treatment be withheld from prospective mothers who have previously borne syphilitic children but who show no stigmas of the disease.

FRANK SPIELMAN.

**Powell and Davey:** A Case of Post-Partum Anemia. *British M. J.* 2: 1131, December 22, 1928.

A woman, aged thirty-five, who had no previous illness (except appendicitis, cured by operation at age of twenty-three) was delivered of her first child in 1918. Labor lasted three days and was followed by a severe postpartum hemorrhage. Baby lived only a few hours. Patient ran a temperature for several weeks, was anemic and suffered with severe headaches. Coli found in urine at that time. A right iliac pain for three months following was attributed to a right ovaritis.

A few days before last pregnancy, November 3, 1926, coli bacilli again found in urine, for which urotropin was administered. Delivery was a breech, apparently normal, placenta was delivered easily. No postpartum hemorrhage. The next day she had severe frontal headache and looked alarmingly anemic. Blood picture of the pernicious type, at that time was: Hgb. 34; R.B.C. 1,603,000; color index 1.1; W.B.C. 6,500; P.M.N. 70.3 per cent; Lymph. 20.3 per cent; Large mono. 4.7 per cent; Eos. 4.0 per cent; Mast cells 0.7 per cent. Physical examination negative. Two blood cultures negative. Temperature rose to 101°. About three weeks postpartum blood picture was: Hgb. 25; R.B.C. 1,290,000; color index 1. Gastric content was devoid of any HCl. The patient was transfused with 470 c.c. citrated blood and felt much better. Gastric content several days later showed achlorhydria. Patient is now twenty-three months after the confinement, apparently in perfect health taking hydrochloric acid regularly. The blood shows no evidence of pernicious anemia.

The case described fulfills all the conditions necessary for a diagnosis of true pernicious anemia. Larrabee (1925) reported 17 cases of severe anemia shortly after pregnancy, not attributable to other causes. In eight of these the blood pictures were of the pernicious type; only four were transfused and recovered, three of the others died. One transfusion may check the progress of the disease. In others, repeated transfusions may be necessary.

ADAIR AND LAUGESON.

**Balfour, Margaret I.:** The Anemia of Pregnancy. *Indian Med. Gazette*, 62: 491, 1927.

It has long been known that severe anemias occur during pregnancy, but it is only since the beginning of the present century that a distinction has been made between the anemia of pregnancy and ordinary pernicious anemia. The main points which indicate the difference in the former are the shorter duration, the absence of marked remissions and exacerbations, and the frequently favorable termination when the pregnancy is ended. Modern medical literature refers to the disease with increasing frequency. Only Bombay cases, 150 in number, are referred to in the article.

In more than half the cases a definite history of sudden onset was given, with various symptoms, pyrexia, enlargement of the spleen, edema, diarrhea, vomiting, other than the vomiting of pregnancy, sore tongue, epistaxis, and weakness. The patient usually entered the hospital in a condition of severe anemia after a month

or six weeks' illness. With rest in bed, good diet, injections of iron and arsenic, some patients improved but frequently there was no improvement. Delivery was usually premature. In some nonfatal cases recovery was rapid after delivery, while in others the anemia lingered. Forty-two per cent of mothers died and 53 per cent of infants were stillborn, while 15.3 per cent of infants died a day or two after birth. The etiology is not known.

C. O. MALAND.

**Broich, H.: Severe Epistaxis During Pregnancy.** *Monatschr. f. Geburtsh. u. Gynäk.* 71: 25, 1925.

Mild epistaxis is a rather frequent occurrence during pregnancy, due to a physiologic swelling of the nasal mucosa. Even large nosebleeds may produce no disturbance in the healthy gravida as exemplified by two cases reported by the author. A few authors have described a disease called pernicious-like anemia of pregnancy. In these patients nosebleed is a frequent symptom. The cause of this anemia is a pregnancy toxemia. Another type of anemia is due to chronic essential thrombopenia. In these cases of anemia, termination of pregnancy is indicated. In cases of thrombopenia operative procedures are dangerous because of the increased bleeding time. Attempts should be made to check hemorrhage by injections of corpus luteum extracts and coagulants. Transfusion of large amounts of blood is useless because the transfused blood is destroyed within twenty-four to forty-eight hours. In cases of chronic anemia small transfusions of citrated blood are much more effective. The author used 15 c.c. of the husband's citrated blood as a trial biologic transfusion, but the patient died three hours after the injection. Hence an intravenous transfusion of even a very small amount of blood should be done only for a very strict indication.

J. P. GREENHILL.

**Rosenloecher, K.: Edema of the Uvula Immediately after Labor.** *Monatschr. f. Geburtsh. u. Gynäk.* 79: 197, 1928.

Hofbauer was the first to point out changes in the pharynx during pregnancy. He found small celled lymphocytic infiltration, superficially and deep, associated with vascular dilatation and edema of the tissues. The author reports a case of edema of the uvula which occurred about fifteen minutes after the spontaneous birth of a child. The entire labor had lasted twenty-three hours. The first symptoms were dyspnea and mild cyanosis. Inspection of the throat revealed the uvula swollen to the size of a thumb, pale red in color, and rubbery in consistency. The tongue and gums appeared normal. Ice was administered and gargles of astringent solutions were used. The symptoms disappeared after fifteen to twenty minutes and the uvula regained its normal size in forty-eight hours.

J. P. GREENHILL.

**Spiegler, R.: Bronchial Asthma and Pregnancy.** *Monatschr. f. Geburtsh. u. Gynäk.* 79: 193, 1928.

The author reports two cases of bronchial asthma in the first of which the asthma disappeared completely during pregnancy whereas in the second the asthmatic attacks returned with the onset of pregnancy after an absence of one year. In the latter case, the asthmatic affliction vanished after the sixth month. This observation furnishes further support for the contention that the vegetative nervous system can produce abnormal reactions during the first half of pregnancy.

J. P. GREENHILL.

Hoehne: The Care of Edema of the Vulva in Pregnancy. *Deutsche med. Wchnschr.* 51: 57, 1925.

This is a report of 5 cases of excessive edema of the vulva. In the first the skin became necrotic and infected; labor was normal but the patient died from a streptococcus infection of the vulva and peritoneum. In the second case a simple cesarean was planned but the skin broke down and a Porro operation had to be done. In the third case an extraperitoneal cesarean was done before the skin had broken down, with satisfactory result. During this operation a large amount of fluid was drained from the vulva tissues. The fourth patient had nephritis and fluid was pouring from an ulcerated place caused by pressure in the left small labium. A transperitoneal cesarean in the lower uterine segment was done, the mother making a good convalescence but the child dying of pneumonia. The fifth case had enormous edema of the vulva at the end of the eighth month. The author made a transverse incision above the pubes on the right, applied pressure to the whole vulva for half an hour, squeezing a large amount of fluid out through the wound, then closed the wound leaving a rubber tissue drain, and continued pressure on the vulva. During the next two days fluid drained out, the vulva edema went down to a large extent, and then was kept within reasonable bounds by pressure compresses until delivery. She was delivered normally and made a good recovery.

Such excessive edema is dangerous because of the likelihood of necrosis and infection. The treatment as described in the last case is efficient.

F. A. PEMBERTON.

Balard, P.: Treatment of Suppurations on Vulva and in Vagina during Pregnancy and Labor. *Rev. franç de gynéc. et d'obst.* 19: 465, 1926.

The author reports 33 cases of suppuration of vulva or vagina during gestation. Most frequent were Bartholin gland abscesses and suppurating vaginal cysts.

During labor Bartholin abscesses form only a slight obstacle due to edema but they favor perineal lacerations. Since serious consequences may arise in the puerperium, the author advises removal of these abscesses between the second and sixth months. Extirpation of the gland done at such times never was followed by interruption of pregnancy but when the infected gland was removed between the seventh and ninth months, premature labor resulted in a few cases, and one patient died from infection. Opiates should be given before and after the operation to prevent the premature termination of pregnancy. If no operation is performed, hot, moist dressings should be applied, vaginal douches given and vaccinothrapy used.

Pregnancy favors the enlargement of vaginal cysts and predisposes them to inflammation and suppuration. Labor often causes a rapid increase in their size. Unless very large, vaginal cysts do not interfere with pregnancy but they may cause dystocia. They usually require no treatment and often rupture spontaneously.

Infection following a ruptured suppurating vaginal cyst is rare. The benignity of this condition, therefore, contraindicates any intervention during pregnancy. During labor, if there is dystocia, the cyst may be punctured.

J. P. GREENHILL.

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## Original Communications\*

### THE PATHOLOGIC DIAGNOSIS OF EARLY CERVICAL AND CORPOREAL CANCER WITH SPECIAL REFERENCE TO THE DIFFERENTIATION FROM PSEUDOMALIGNANT INFLAMMATORY LESIONS

By EMIL NOVAK, M.D., BALTIMORE, MD.

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IN A RECENT paper<sup>1</sup> before the Southern Surgical Association, I discussed the importance of biopsy and diagnostic curettage in the recognition of early uterine cancer, and urged that the prevalent conception as to the pathology of uterine cancer needs freshening. The physician who in his mind associates this disease with a cauliflower growth of the cervix, or with a foul, excavated crater ulcer, is apt to feel relieved if his examination of the patient with a suspicious history shows no such lesions. And yet, in just such cases, the cervix may furnish perfectly valid, though not so obvious, evidence to warrant the diagnosis, or at least the strong suspicion, of malignancy.

It is these earlier pictures of malignancy, therefore, with which the profession should learn to familiarize themselves, for it is from this early group that we can hope to garner a considerable proportion of cures. A fair analogy may be drawn with the changed concept as to the clinical picture of other diseases, such as appendicitis. One no longer withholds his diagnosis until, as was at one time the case, the patient exhibits abdominal distension, persistent vomiting, profound prostration, a hippocratic facies, and other evidences of a peritonitic sequel of the original disease. Similar comparisons might be made with other conditions.

\*All of the papers included in this issue of the Journal were read at the Fifty-fourth Annual Meeting of the American Gynecological Society, Old Point Comfort, Va., May 22-24, 1929. The remaining papers and discussions will be printed in the November issue.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

There can be no doubt that the educational campaign against cancer is bringing an increasing number of cases to the physician in an early, favorable stage of the disease. The physician must be prepared to do his part by recognizing suspicious lesions, and by seeing that each patient's individual problem is authoritatively settled, as, with rare exceptions, it can be. It is the gynecologist who will be called upon for this responsible task, which he must undertake either alone or with the collaboration of a skilled pathologist.

More and more, as cases come earlier, the microscope will be called upon to make, rather than merely to confirm, the diagnosis of uterine cancer. Difficulties in the diagnosis of late cancer are as rare from the pathologic as from the clinical standpoint. When dealing with early lesions, those which clinically are usually only suspicious of cancer, the microscopic interpretation is not always so easy, although, with comparatively few exceptions, the well-equipped pathologist can decide the question correctly.

The microscopic characteristics of cancer in the outspoken case are so clearly defined that the diagnosis is a purely objective one, in which all pathologists agree. With a certain group of borderline cases, on the other hand, it is hard to keep out the subjective factor, for pathologists will differ in their interpretations as to what constitutes good microscopic evidence of beginning malignant transgression of epithelial tissue. The term *borderline*, in this connection, is used from the standpoint of interpretation and not to indicate that one is actually dealing with an intermediate stage between benign and malignant disease.

In my previous paper, already referred to, I stressed the fact that, because of the rather specialized physiologic and pathologic variations in structure encountered in the uterine mucosa, the gynecologic pathologist, who has daily opportunities of studying such lesions, has some advantage over the general pathologist. To put it another way, a man may be an excellent general pathologist, in the ordinary sense of the term, and yet go wrong rather easily in the interpretation of many of the lesions of the genital organs.

It is scarcely necessary here to elaborate upon the pathologic criteria of malignancy in general. From the standpoint of microscopic examination, they fall into two groups, viz.:

(a) *The General Pattern*.—The general impression which is given by the low-power examination suffices to make the diagnosis in most cases of cancer, but this, on the other hand, may not be conclusive in the early or doubtful case, as will be discussed later. Under this head comes also the question of the invasiveness or noninvasiveness of the epithelial growth, which, in the borderline case, may not be of much assistance in making the diagnosis. For that matter it is not uncommon in many sections of undoubted cancer, particularly with adenocarcinoma of the uterus, to observe no evidence of penetration of the basement membrane, or invasion of the underlying tissue. In the lat-

ter sense there is commonly far more invasiveness to be seen in the perfectly benign adenomyoma. Finally, in making diagnoses from uterine scrapings, in which one has to deal with fragments of mucosa alone, one can expect little help in deciding as to whether or not the disease is invasive of the musculature.

(b) *Atypical Characters of the Epithelial Cells.*—In the more obvious stages of cancer, the high power picture is apt to be studied chiefly to confirm the impression of malignancy already obtained from the low power survey. When the latter is inconclusive, however, as it is apt to be in the early or borderline cases, one must concentrate, in a very analytic way, upon the finer study of the cell characteristics. Lack of differentiation of the cells as compared with the normal prototype, and such nuclear abnormalities as mitoses and hyperchromatosis are especially important. In the nonmalignant hyperplasias such changes are not in evidence, although misleading pictures may be encountered. For example, as I shall discuss later in this paper, one may find heavily stained nuclei and perhaps even an occasional mitosis in certain inflammatory lesions of the cervix which are definitely benign.

#### THE DIFFERENTIATION OF CERVICAL LESIONS

It is in the cervix that one most often encounters pictures calling for careful differentiation. Certain benign lesions, especially those of inflammatory character, not infrequently give rise to gross appearances which suggest malignancy so strongly that no clinician should be willing to assume the responsibility of making the decision without the aid of the microscope. This is particularly true of cervical polypi and chronic endocervicitis, especially when in association with either erosion or ectropion. The latter is, of course, most often seen with lacerations. In cases of this sort, the everted mucosa is not infrequently red and granular, and perhaps bleeds on slight touch. (Fig. 1.) Moreover, it may show a definitely papillary or sprout-like tendency, and, on palpation, may give a sense of definite induration.

Clinically, such lesions belong in the category labelled suspicious, and I know of no other way in which the decision can be made than by biopsy and microscopic examination. For a discussion of this procedure I would refer to my previous paper, in which I have also discussed the question of the alleged danger of disseminating cancer cells by biopsy, or by diagnostic curettage.

The evidence for such a danger is far from convincing, but even if there were some danger, it would be far less, in my judgment, than to leave the issue in the individual case undecided or decided wrongly. How else can the decision be made in these clinically doubtful cases than by means of biopsy? To treat such cases conservatively would probably spell death to the patient if the lesion be actually malignant. On the other hand, to decide that radical treatment is advisable because

the lesion, if not cancerous, is at any rate "precancerous," is slipshod and unscientific. It may entail for a lesion that is perfectly benign an unnecessary and more or less dangerous operation, or unnecessary and more or less distressing radium therapy.

The microscope will settle the question in all but a very small proportion of cases. A good frozen section will usually suffice, for cervical biopsy tissue is well adapted for frozen section work. If there is any doubt, good sections by the permanent technic are of course desirable before deciding on the plan of treatment.



Fig. 1.—A lesion of the cervix which clinically was strongly suspicious, and in which biopsy showed the cancer depicted in Fig. 7. Panhysterectomy and double salpingo-oophorectomy were done (the adnexa were cut away in order to search for ova in the tubes).

From a microscopic standpoint, inflammatory lesions of the cervix may be confused with either squamous cell carcinoma or adenocarcinoma, though more frequently with the former. The reason for this is that chronic inflammation not only leads to the so-called "epidermization" of the cylindric epithelium, but excites the squamous epithelium, normally limited to the surface, to an invasion of the stroma. A section of such a cervix will often, therefore, reveal cell nests and

columns of squamous epithelium in the depths of the stroma, producing a picture not unlike that seen with squamous cell carcinoma. Many mistakes in diagnosis have been made because of this, but error can be avoided if one understands the mechanism, characteristics and significance of this invasion of epithelium. For the elucidation of this we are indebted chiefly to the investigations of Meyer,<sup>2</sup> although such pictures had been described by Ruge,<sup>3</sup> and many others, before him.

For a proper understanding of this question, it is necessary to bear in mind the development of the epithelial lining of the uterine and cervical canals. All of the genital epithelium, with the exception of



Fig. 2.—Showing manner in which creepers of the basal layer of stratified squamous epithelium push beneath the cylindric epithelium (*a*). In other places (*c*) there are several layers of stratified epithelium beneath the cylindric, and the cells of the latter are becoming flattened (*b*) or degenerated (*c*). A high power picture of the same field is shown in Fig. 3.

that covering the lower portion of the vagina, is ultimately derived from the same mother tissue, i.e., the celomic epithelium. By the third or fourth month of fetal life the differentiation between the cylindric epithelium of the uterine canal and the squamous epithelium of the pars vaginalis is quite distinct. It is important to note, too, that the line of transition between the two types is not at the external os, but well within the cervical canal. This is due to the manner of formation of the vaginal fornices, which are developed in the zone of squamous epithelium.



At a later stage, put by Meyer at about the sixth or seventh fetal month, the secretory activity of the cylindric epithelium becomes manifest. The destructive effect of the secretion pushes the squamous epithelium out to the region of the external os. Often, indeed, it is crowded even further out, so that cylindric epithelium covers an areola of variable size about the os. Thus is produced the so-called congenital erosion.

The explanation which Ruge gives of this epithelial interplay, and of the formation of congenital erosions, differs from that of Meyer, but I believe the latter to be the correct one. It is not easy, however, to understand how the mucinous secretion of the cylindric epithelium exerts such a destructive effect upon the squamous epithelium, and it



Fig. 3.—High power of areas represented in Fig. 2.

seems possible that some other factor, as yet unknown, may be more important.

The same interplay of the two types of epithelium is seen in later life, under the influence of inflammatory irritation. As a first stage in endocervicitis there is produced a hypersecretion of the cylindric epithelium and an extension outward to the pars vaginalis, with the production of an erosion. In this stage, which Meyer calls the first healing stage, the erosion is covered with a cylindric epithelium. The latter still retains its gland-forming tendency, so that new gland invaginations may be formed far out on the pars vaginalis. As the inflammation recedes, the squamous epithelium again asserts itself, pushing back the cylindric epithelium to the region of the external os.

It is during this, the second healing stage, that one observes the squamous cell invasion below the surface with which we are especially concerned in the differentiation from cancer. Long tongues of squamous epithelium creep along the basement membrane, lifting and often destroying the cylindric epithelium (Figs. 2, 3, and 4). It is common to see this invasion beneath the gland epithelium. Often, instead of a stratified squamous epithelium, one sees only the basal layer of the latter creeping along beneath the gland epithelium, giving an appearance of stratification to the latter (Figs. 2, 3, and 4). As the process advances, the entire gland lumen may be filled with the stratified squamous epithelium, and the cylindric epithelium, as it were, choked



Fig. 4.—Showing, above and to left, a nest of epithelial cells resulting from an advance of process described in Fig. 2, the gland lumen being entirely filled, and the columnar epithelium being choked off. The gland below this, and also the one to the right, show a less advanced stage of the same process, with some of the columnar cells still persisting. In lower left-hand corner is a fenestrated gland picture, produced by a combination of the same change with the adenomatous reduplication of the cylindric epithelium often seen in inflammatory lesions. No evidence of malignancy in any of these areas (see text).

to death (Fig. 5). In the latter case, the plugs of squamous epithelium often exhibit small central gland-like cavities filled with mucinous substance, as can be demonstrated by differential staining. In less extreme areas, the cylindric epithelium may still be demonstrable.

Such pictures may lead to a strong suspicion of adenocarcinoma, and I know of several instances in which the mistake has been made. The changes which have been described may in long-standing cases alternate repeatedly, and different phases may be observed in different parts of the cervix at one and the same time.

From what has been said, it will be seen that this invasion of the depths by creepers of squamous epithelium takes place characteristically on the trellis furnished by the gland framework (Fig. 4). This, as Meyer emphasizes, is one of the most important points in the differentiation from cancer. The penetration of actual cancer may of course involve the glands also, but this invasion is a more ruthless and less orderly one, and is not of course confined to the gland elements, as with the inflammatory process just described (Fig. 6). With the latter, the surface epithelium is normal, or at any rate, shows no sign of malignancy. With cancer the surface epithelium is usually distinctly atypical, and frequently has been lost by ulceration. In the

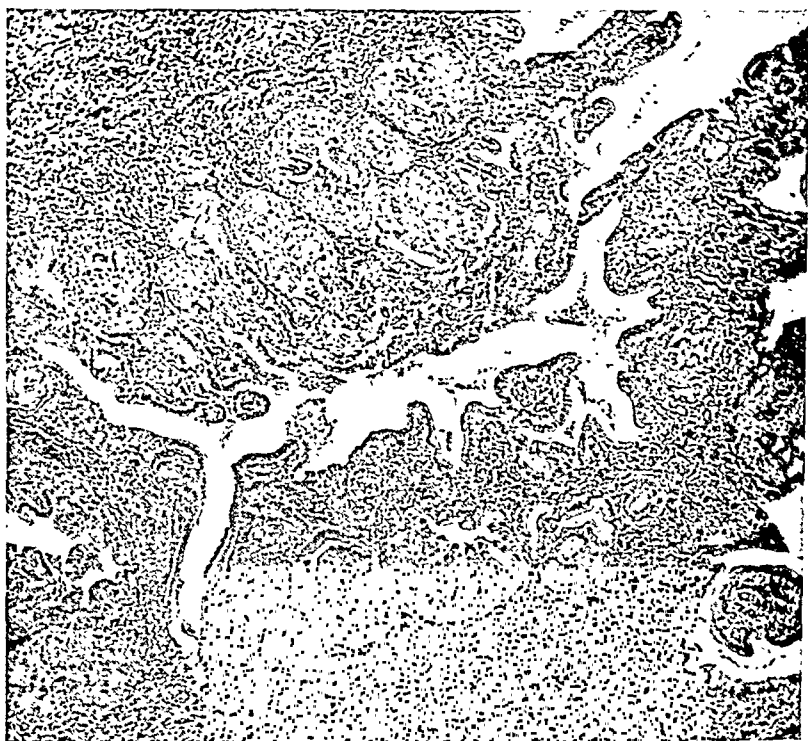


Fig. 5.—Pictures like this, not uncommon, might readily be mistaken for cancer. The patient was twenty-six years old, and has remained perfectly well after simple excision of the cervical polyp from which this was taken. The cell nests beneath the columnar epithelium are due to the same benign extension of the squamous epithelium depicted in the preceding pictures. The constituent cells show none of the characteristics of cancer cells. The overlying columnar epithelium is likewise normal, except for some flattening and degeneration.

cancerous process, nests of atypical epithelium are to be seen invading the stroma everywhere, and, except in the earliest stages, usually more extensively than one sees in the inflammatory process. In the latter, it is true that in individual sections many of the nests appear to be quite independent of the gland structure, but, with some exceptions, serial section study will show that this is not the case. A study of the invasive process in the glands themselves shows how easily one may be misled by the angle of section.

It should be added that the above explanation of this process, as championed by Meyer, and with which my own observations lead me to agree, is not the only one which has been suggested. There are still some who believe that there is, in these cases, a genuine metaplasia of the cylindric to the squamous type of epithelium. The chief support for this, it seems to me, would come from the not infrequent finding of squamous epithelium in gland epithelium far removed from the surface, and showing no connection with the latter even by outriders of the basal layer of the squamous epithelium.



Fig. 6.—Early squamous cell cancer in a patient with only suspicious cervical lesion in which no biopsy was done. The diagnosis was made after and not before the operation, as might have been done. Note the difference between these cell nests and those shown in Fig. 2. Under the high power the cells are seen to be closely packed, placed chiefly like palisades perpendicularly to the basement membrane, and showing the usual cancer characters (mitoses, hyperchromatosis, etc.). The cell nests here are independent of the glands, although of course glands are often invaded in cancer also.

Such pictures Meyer would explain on the ground that, with the interplay of epithelium produced by inflammatory disease, rests of squamous epithelium are left stranded, so to speak, beneath the cylindric epithelium, developing active growth later on. Although he has demonstrated islands of cells which he interprets in this way, it seems to me that the evidence on this point is somewhat less convincing than that bearing on other features of the general process. In spite of

Meyer's emphatic declaration to the contrary, I am inclined to believe, with Ruge, that in the cervix, as in the body of the uterus, genuine metaplasia of cylindric to stratified squamous epithelium may at times occur, though not vice versa. Moreover, pictures are at times observed which suggest that there is a marked dipping in of the squamous epithelium independent of the gland invaginations, and suggesting a benign prototype of the scharlach-R cancer described by Fischer.

After all, however, the differentiation of these inflammatory lesions from very early cancer is based upon the study of the cells themselves



Fig. 7.—Section from uterus represented in Fig. 1, showing benign inflammatory "metaplasia" on one lip (left) and definite cancer on the other (right).

rather than upon such differences in general architecture as have been discussed (Fig. 7). In the diagnosis of cancer beyond the earliest stages, of course, the general pattern suffices to make the diagnosis for the trained microscopist. A glance through the low power lens is often all that is needed, the high power being used merely for confirmation and finer study. When dealing with very early and doubtful cases, however, every possible resource must be made use of, and even then there will remain a small residuum of cases in which a positive diagnosis cannot be made.

Even though numerous cell nests are found in the stroma, cancer would hardly be thought of if these cells show a perfectly typical structure, i.e., if they are of uniform nuclei, and with no evidence of mitoses, hyperchromatosis, and other nuclear changes suggestive of malignancy. Another point of differentiation is the fact that in the benign lesion it is only the basal cells of the epithelium which are arranged perpendicularly to the basement membrane, like palisades; while in cancer this perpendicularity is often noted in the upper layers as well. In the majority of instances the diagnosis is easy, especially when based upon a thorough study of the entire section, or preferably of a number of sections. The clinical history, especially as to the age of the patient, the gross appearance of the lesion, and the presence or absence of bleeding, are of great auxiliary importance, and certainly the pathologist is entitled to all such data when asked to pass upon the question of malignancy or nonmalignancy.

In a small proportion of cases the epithelial cells of the surface, or those in cell nests beneath the surface, present an intermediate sort of picture which makes the decision extremely difficult or perhaps impossible. The stratification of the epithelium of the surface may be well preserved, but the cells may be somewhat more compactly packed. The nuclei, especially of the basal layers, may be large and heavily stained, and rarely a few mitoses may be observed. It is of course the basal layer from which regeneration normally takes place, but mitoses are almost never seen in this layer under normal conditions or even in inflammatory lesions. They are even more rare in the superficial layers, and I do not recall ever having seen them in these strata except in malignancy. To deny, however, that in the occasional case, one may find such mild evidences of nuclear activity as above mentioned, even including an occasional mitosis in the deeper layers, would be unjustified.

The same difficulty is encountered at times in inflammatory lesions in interpreting the pictures presented by the cell nests in the stroma. When the section has passed through the basal layers, one may find the same dark, heavily stained nuclei and the same rather compact epithelium above mentioned. Other areas, however, may show a more distinctive picture, and the surface epithelium may be quite normal in appearance. Numerous sections are advisable before arriving at a final diagnosis in this, perhaps the most difficult of all groups.

Just what to do in cases where a definite doubt exists must, I think, depend upon the circumstances of the individual case. If the patient be comparatively young and the gross lesion not especially suspicious, treatment should be expectant, with repetition of the biopsy within a few weeks. If, on the other hand, the lesion be distinctly suspicious, even microscopically, and the patient be of the cancer age, there are many who would feel justified in instituting the usual treatment for

cancer, either radium or surgery, depending on circumstances and predilections. If operation is done, the diagnosis can usually be definitely established from the extirpated uterus, and in a considerable proportion, perhaps the majority, of such cases, malignancy will not be found. With radium, on the other hand, such a check-up is not possible, and hence the accuracy of the pathologic control of such cases is obviously less to that extent. It should again be emphasized, however, that only a small proportion are of this type, i.e., both clinically and pathologically doubtful, and that in the great majority of instances, accurate diagnosis is possible from biopsy sections.

There is one other benign picture which merits mention, because of its great frequency and the fact that it is not so rarely falsely diagnosed as cancer, in this case adenocarcinoma. I refer to the fenestrated, acinous appearance seen so often with inflammatory lesions, and especially in polypi, and which is well shown in Figs. 4 and 5. This picture I believe to be due to two factors. The stratification is unquestionably the result of the aggressive overgrowth of the stratified squamous epithelium which has been described already. There is, however, apparently a genuine increase in the number of gland lumina, which I believe to be due to the adenomatous tendency of the cervical epithelium under the influence of inflammation. In chronic endocervicitis one commonly observes that the epithelium on the surface, instead of being perfectly smooth, exhibits a very wavy outline due to this invaginating tendency. In more marked stages, the adenomatous tendency is undoubted, almost suggesting that so characteristic of the histologically similar lining epithelium of a pseudomucinous cystadenoma of the ovary. The gland-forming tendency is exhibited also by the epithelium lining the glands, so that complicated patterns, like lace-work, are often produced. And yet the cylindric epithelium, when not smothered by the squamous, is of one cell thickness, often somewhat flattened, with no suggestion of malignancy.

#### THE DIFFERENTIATION OF ENDOMETRIAL LESIONS

In cases of uterine bleeding which present no incriminating gross findings or symptomatic features, and especially when the cervix reveals no suggestion of malignancy, diagnostic curettage is of decisive importance in a very large proportion of cases. Not infrequently the gross appearance of the tissue removed by the curette is sufficiently characteristic to permit of reasonably accurate diagnosis. When the curettings are abundant and contain rather large bits of tissue, satisfactory frozen sections can be obtained for diagnosis or confirmation. This will prove to be the case in most cases of cancer, so that, if the naked eye and the microscopic findings both indicate cancer, the surgeon can feel entirely safe in proceeding with radical operation under the same anesthesia. The advantages of this are obvious.

If, however, the curettings are scanty and not characteristic, satisfactory frozen sections are difficult to obtain, and it is wise to wait for fixation of the tissue by one of the permanent technics. In most cases, however, cancer will not be found, so that another anesthetic is not necessary except in the unusual case of very early carcinoma.

From a microscopic standpoint the diagnosis of the great majority of cases of adenocarcinoma of the uterus presents no difficulty. In the early cases it is of importance to examine all the tissue removed, and to make a number of sections at various levels in the block. Otherwise the early, localized lesion may easily be missed.

Inflammatory lesions of the endometrium rarely give rise to pictures which might lead to confusion in the diagnosis, whether or not the cause of the inflammation be a retention of gestation products. In the latter case there are usually telltale bits of evidence in the presence of chorionic villi, decidual cells, etc. With chronic inflammation of marked degree there may be some distortion of glands, but the picture does not in any way suggest malignancy. The interstitial inflammatory process usually dominates the picture, the glands often being pushed apart or distorted because of this. Epithelial changes suggestive of malignancy are absent.

With benign hyperplasia and polypi there is at times some difficulty in making the diagnosis. The very nature of hyperplasia suggests a proliferative activity of the epithelial as well as the stromal elements. A single section may not show the characteristic Swiss-cheese pattern, which would at once give the clue. It may reveal only a mass of rather thickly crowded glands, in some of which the epithelium may be much thickened, with dark heavy-staining nuclei. This is not an uncommon finding, for in some areas of the hyperplastic endometrium the glands may be thickly crowded together. Mitoses may be numerous, although this means very little in a tissue which, because of its cyclical regeneration, shows a greater or less number of mitoses as a normal finding. Pictures like those just described have more than once been wrongly diagnosed as "adenoma malignum." At times, it is difficult to be sure of the diagnosis from the single section, although almost always other sections will reveal a more or less distinctive picture, clearing up the diagnosis satisfactorily. In a small proportion of cases, however, the diagnosis must remain doubtful and a repetition of the curettage is advisable after a few weeks.

There is one other occasional finding which has been much discussed and which may puzzle the microscopist who is not familiar with it. I refer to the so-called "epidermization" of the endometrial epithelium. This squamous cell transformation of the normally cylindric epithelium may be occasionally seen not only in undoubtedly benign lesions, but, in my experience, is much more common in adenocarcinoma of the



body of the uterus. It occurs, too, in adenocarcinoma of the cervix. There can be little doubt that it explains most of the cases which have in past years been reported as instances of combined squamous cell and adenocarcinoma. (Fig. 8.)

The occurrence of "epidermization" in benign lesions of the endometrium is, however, far less frequent. Fluhmann,<sup>4</sup> in a recent study of the literature, was able to collect only 5 cases in addition to his own, but I believe that the occurrence is not quite so rare as these figures

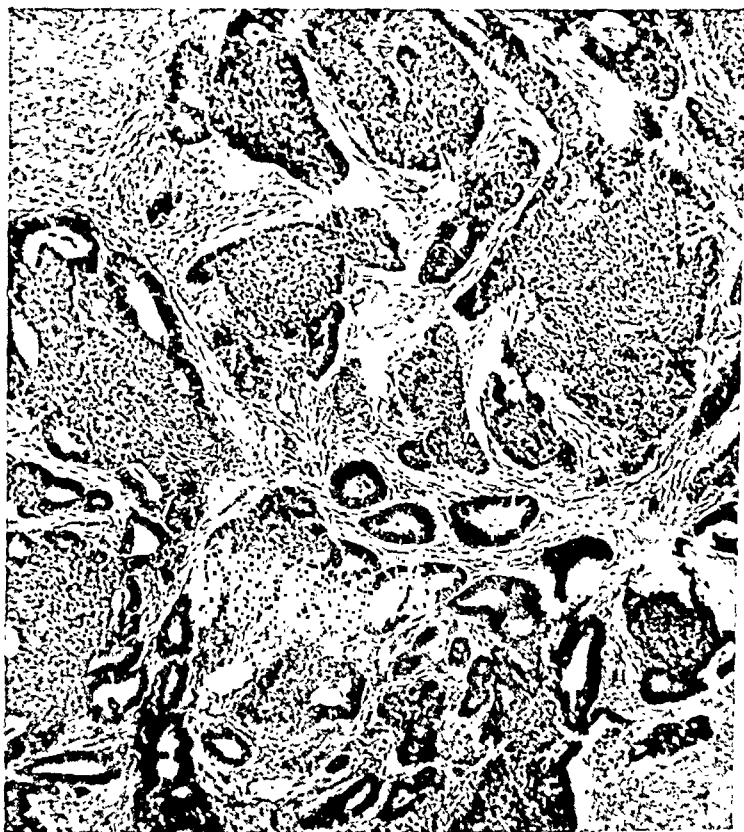


Fig. 8.—Extensive squamous metaplasia in an adenocarcinoma of the uterus. Here there is no doubt of the transition from a primarily gland carcinoma, but in other areas the squamous change is so extensive that the primary character of the tumor is blotted out. Such cases have in the past often been wrongly interpreted as combinations of squamous cell and adenocarcinoma.

would indicate. I have found this picture in several cases, most recently in the one which is illustrated in Figs. 9 and 10. Hintze,<sup>5</sup> in a recent report, described 9 cases encountered in one laboratory within a period of five years, and collected a number of others, some of which had not been included in Fluhmann's collection.

There has been considerable discussion as to the etiology and the significance of this "epidermization," or "epidermoidization," of the endometrium. The view has been held by some that this epithelial change is due to the fact that some of the cells in the regenerative

layer retain their indifferent characteristics, being thus capable of developing into either squamous or cylindric epithelium. Meyer, indeed, has described collections of such cells in the uteri of newborn children. So far as I know, however, they have not been observed in the adult uterus, and they would probably soon be lost as a result of the desquamative changes of menstruation and pregnancy. There can be little doubt, therefore, that the "epidermization" represents a genuine metaplasia of cylindric to squamous epithelium.

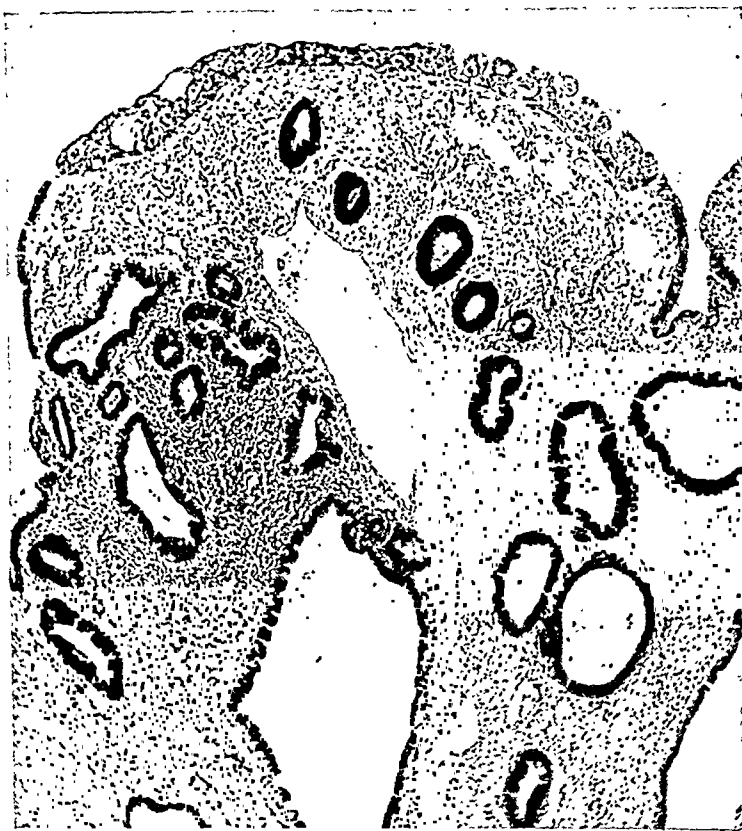


Fig. 9.—Squamous "metaplasia" or "epidermization" of the surface epithelium in a case of hyperplasia of the endometrium and adenomyoma. This is a purely benign change, although in this case a hysterectomy was done for other indications. The patient, aged twenty-three, has remained perfectly well.

As has already been emphasized, the celomic epithelium is the common progenitor of both cylindric and squamous epithelium within the genital canal, and hence it is not surprising that a certain degree of interchangeability of such tissues persists, capable of exaggeration under certain conditions. The strongly proliferative tendency characteristic of hyperplasia, and, of course, even more of cancer, would seem to explain the fact that it is in these two conditions that the metaplasia is observed almost exclusively. A similar epithelial change, however, was described by Mainzer following formalin vaporization of the

uterine cavity, and has been noted also in gonorrheal and other forms of endometritis (Wertheim and Menge), endometrial tuberculosis (von Franque and others). Such a metaplasia, too, was produced by various irritants in the bladders of rabbits (Lubarsch) as well as in the stomachs of the same animals (Fütterer). Oeri, again, speaks of squamous and even cornified epithelial areas in the mucosa of nasal polypi; and also in the mucosa of the larynx, trachea and bronchi. The process has also been noted in the mucosa of the gall bladder, and has been recently described in the ducts of the pancreas. There is nothing surprising, therefore, in the occurrence of such squamous metaplasia in

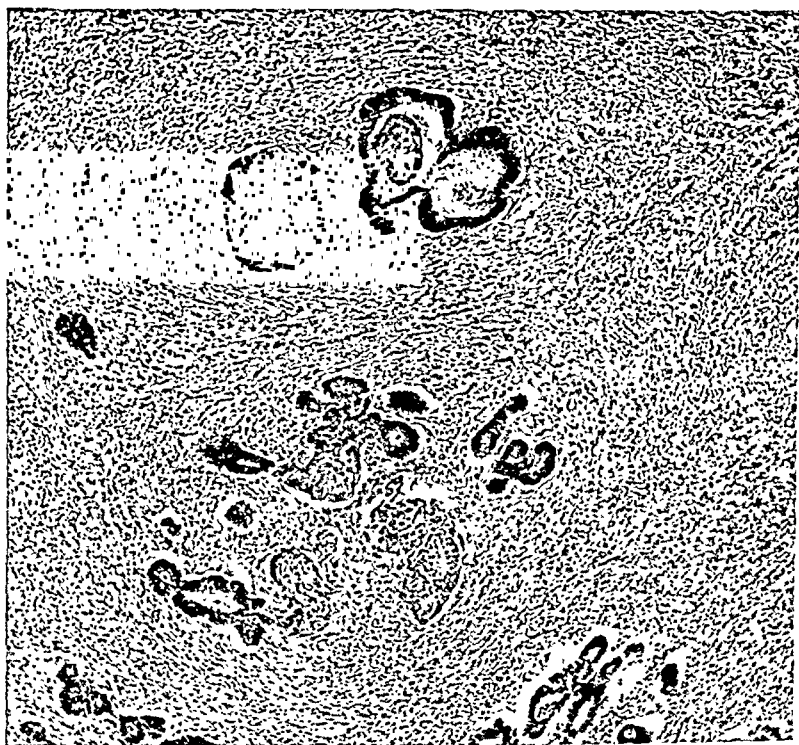


Fig.10.—“Epidermization” of deeper lying gland epithelium of adenomyoma in same case. These changes, formerly considered as evidence of malignancy, are now looked upon as definitely benign (see text).

the endometrium, where, as a matter of fact, the kinship of the two types of epithelium is closer than elsewhere.

While many of the early writers looked upon “epidermization” as indicative of malignancy, the evidence is now quite convincing that in itself it is an essentially benign process. For example, the endometrium pictured in Figs. 9 and 10 was derived from a patient aged twenty-three, with no evidence of malignancy, although a hysterectomy was done for other indications. Of Hintze’s 9 cases, simple curetting was done in all but 2, but all had remained well at periods of from two to five years after operations.

## GENERAL CONSIDERATIONS

From what has been said I believe that the emphasis which I have placed upon a really authoritative pathologic examination has been justified. Unless the one called upon to make these diagnoses is not only a competent general pathologist, but is also familiar with such rather specialized pictures as we have been considering, grave mistakes will be made, as they have often been made in the past. On the other hand, the clinician, aside from his general responsibility in the individual case, must not only recognize when the help of the pathologist is needed, but must collaborate with him by supplying tissue from which a diagnosis can really be made.

The tissue in biopsy can be removed by means of a sharp knife, after which the edges of the wound are seared with the cautery. Removal with the cautery knife alone is not so satisfactory, as the small bit of tissue is thereby cooked and shriveled, rendering it valueless for microscopic examination. At times the knife may prove a rather awkward instrument for biopsy, especially when the vagina is deep and when the cervix tends to slip away from the scalpel. In such cases a very useful and convenient instrument is a punch devised for this purpose. It will permit of the rapid biting out of small oval bits of tissue.

Two extra precautions should be urged in the performance of biopsy. First, the excision should be made from the area, perhaps very small, which is most under suspicion, for adjoining parts, in an early cancer, will probably show no evidence of the disease. Second, care should be taken to have the tissue cut at the proper angle in the making of the sections, especially, of course, with a view to showing the mucosa. Where the laboratory man is ignorant of just what the clinician is driving at, and even more in hospitals where the sections are prepared by lay technicians, the section is apt to be cut in such a way as perhaps to show mostly fibrous tissue, with little or none of the mucosa. Negative reports on such sections would, of course, be worse than useless. My own custom is to place the excised tissue on a piece of gauze in exactly the position in which it ought to be cut by the person who is to make the sections. More than one section, moreover, is always desirable, although not always essential for diagnosis.

As I mentioned in my previous paper, the ideal condition of affairs is for the gynecologist to be equipped to make his own microscopic examinations. Such an equipment, not difficult of acquirement to anyone having a ground knowledge of general pathology, is possessed by a certain proportion of gynecologists, but the proportion should be larger. Many otherwise excellent hospital services in gynecology are weakened, it seems to me, by the insufficient stress put upon pathology. Not only is a thorough knowledge of pathology of immediate diagnostic value in such problems as the one we are discussing, but it

broadens and clarifies one's viewpoint on the clinical problems of our specialty as well. No better advice can be given to the young man contemplating a gynecologic career than to become thoroughly and broadly conversant with the pathology of the lesions which he will be called upon to treat. Once such an interest in gynecologic pathology is developed, it will rarely be lost.

The question may fairly be asked, "Are the results of microscopic examination from biopsy and diagnostic curettage sufficiently trustworthy to be used as a guide in the treatment of suspicious cases?" When these studies are made in the manner above outlined I believe that this question can be unhesitatingly answered in the affirmative. The proof of the matter lies, of course, in the subsequent course of cases diagnosed and treated according to this policy. As we have not as yet made a follow-up analysis of our cases, from this standpoint, I can for the present give only impressions rather than actual facts. I cannot recall any case in which a definite diagnosis of malignancy was made from biopsy sections or curettings in which the diagnosis was not confirmed by the examination of the extirpated uterus, when surgery was done. This, of course, does not include a certain number of cases which microscopically were considered only suspicious or doubtful but in which, for one reason or another, a radical operation was done. Nor would it apply to the rare cases, of which I have personally observed none, of adenocarcinoma of the uterus so localized that the lesion was apparently entirely cleared away by curetting. In these, of which a considerable number (between 30 and 40) have been reported, the curettings show definite cancer, while no evidence of malignancy is found in the uterus after extirpation. As hysterectomy is the proper procedure in such cases, anyhow, the value of the preliminary diagnostic curettage in revealing cancer this early is all the more evident.

Several instructive follow-up studies have been made by others which justify the confidence which most of us place in the microscopic examination of doubtful cases. Hirschberg,<sup>6</sup> in 1925, reported upon the subsequent course of 116 cases in which biopsy had been done, and 244 in which diagnostic curettage had been performed. In these groups are included 7 cases in which the diagnostic procedure showed the incorrectness of a more or less definite clinical diagnosis, viz.: 3 biopsies revealing no malignancy where cancer of the cervix had been diagnosed, and 4 curettings revealing a benign lesion of the endometrium when a more or less definite diagnosis had been made of cancer. Of 107 biopsies upon suspicious lesions of the cervix, 30 led to the histologic diagnosis of cancer, 77 to that of benign conditions. These figures, it seems to me, indicate the diagnostic indispensability of these two procedures in the differentiation of suspicious lesions of either the cervix or body.

Perhaps even more impressive are the results of the follow-up study reported by Meyer and Kaufmann.<sup>7</sup> The biopsy cases numbered 165, of which 146 were clinically suspicious of cancer. Twenty-six of these actually were demonstrated to be histologically cancer, the remainder, 117 cases, being diagnosed as benign inflammatory lesions. Among this histologically benign group were 15 cases which had been considered so definitely cancerous from the clinical viewpoint that the biopsy was repeated once or twice, but with the same result. The remaining 3 of the 146 cases permitted of no diagnosis, because of insufficient or unsatisfactory tissue. On the other side of the picture, 2 cases of definite histologic cancer were revealed in which there was no clinical suspicion of cancer.

The cases of diagnostic curettage, 273 in number, were studied in the same manner. Two hundred and sixty of these were clinically classed as suspicious. Of these 29 proved to be cancerous, 223 benign, and 8 showed insufficient tissue for diagnosis. Moreover, 9 cases of definite cancer were unearthed by curetting and microscopic examination, in which there had been no clinical suspicion of cancer, while 3 cases with a definite clinical diagnosis proved to be benign.

After all, the question of whether a lesion is malignant or benign is determined, as Meyer emphasizes, by its effect upon the patient, i.e., by its subsequent clinical course. With this point in view, a considerable number of cases were studied, by Meyer and Kaufmann, in which biopsy or curetting had been done, and which were traced, where possible, and reexamined. Of 43 cases with a clinical diagnosis of carcinoma, but in which biopsy showed no cancer, all had remained perfectly well after conservative treatment. In the same way, in 107 cases in which diagnosis had been made by microscopic examination of curettings, in not one did the subsequent course belie the histologic diagnosis. This, of course, is a remarkable record, possible only where the clinical and pathologic studies are well coordinated, and where the pathologist is genuinely expert. These results, however, ought to be closely approached in every well organized clinic. Such scientific study of suspicious cases entails no hardship upon either the physician or the patient. It enables us to sift out, with reasonable precision, the cancerous from the noncancerous lesions, and saves many patients from unjustifiably radical procedures on the one hand, or deplorably insufficient procedures on the other.

A third recent study of this type, by Hirsch-Hoffman,<sup>8</sup> may be added to, bearing out as it does the trustworthiness of histologic diagnosis in competent hands. This author, in 1927, studied the case in which in the years 1923 to 1925, a histologic diagnosis had been made of benign cervical erosion. Of a total group of 241, it was possible to reexamine 195. No lesion was found in 152 of these, while in 25

cervical erosion was present. In all these, however, microscopic examination showed the lesion to be benign.

The very recent study of Pemberton and Smith<sup>9</sup> furnishes evidence along the same line. A follow-up of patients who had had cervical operations at the Free Hospital for Women, in Boston, showed that "not one patient whose cervical specimen was suspicious but not malignant has been found to have developed cancer, although sufficient time has elapsed since operation."

Several more points justify emphasis. In the first place, only a comparatively small proportion of cervical lesions call for biopsy. In the overwhelming majority, the diagnosis is reasonably plain from a clinical standpoint, and in these biopsy need not be done, or, if it is resorted to, the evidence afforded by it will usually be only confirmatory. Cancer of the cervix will rarely be found in cases which clinically present no suspicious features whatsoever. But it will not infrequently be found in cases which clinically are only suspicious. Since the vast majority of cases are either obviously benign or obviously malignant, biopsy will be indicated in only a small proportion of cervical lesions, probably less than 5 per cent. In cervical lesions, one has the great advantage of actually seeing and feeling the lesion. This, however, is not true of lesions of the endometrium, so that the proportion of cases in which the diagnosis must be made by the microscope is actually much higher.

Again, and especially in the matter of curetting for diagnosis, there are many cases in which the diagnosis can be made with reasonable certainty by the naked eye appearance of the removed tissue. Hyperplasia of the endometrium, retained gestation products, and adenocarcinoma, to mention only three of the lesions often encountered, all present, in typical cases, more or less characteristic gross pictures, upon which it is not necessary to elaborate here.

Finally, it need scarcely be said that the pathologist, no matter how expert he may be, encounters his pitfalls, like his clinical coworker. There is a small proportion of cases in which our present-day knowledge of cancer diagnosis, as applied to the individual case, simply will not permit of definite decision. In such cases the honest pathologist need not be ashamed to express his limitations. When a diagnosis is thus perforce held in abeyance, it is usually advisable and possible to hold treatment in abeyance also, and to repeat the biopsy or curettage in two or three weeks. In certain cases, the circumstances of the case may make it seem wise to proceed with radical measures on mere suspicion, but this policy should certainly not be made a general rule.

The introduction into clinicopathologic nomenclature of the term "precancerous" has done some good, but, perhaps almost as much harm. The harm has come chiefly from the fact that the frequent resort to radical treatment of lesions which are merely "suspicious"

has been justified in the minds of the offending surgeons on the ground that such lesions are "precancerous." There is no evidence as yet of an intermediate stage between noncancerous and cancerous disease, although there is much evidence to indicate that certain benign lesions, such as chronic inflammation, predispose to the development of cancer. If the term "precancerous" were always used in this sense, there would be little objection to it. But lesions "precancerous" in this sense do not call for radical measures for their removal. Corrective



Fig. 11.—The growing margin of an adenocarcinoma of the body, showing the sharp line between the perfectly benign endometrial glands to the left (some distended by senile obliteration of the ducts) and the definitely cancerous glands to the right. Still further to the right, beyond the limits of the picture, is a large tree-like cancer growth, which shows little or no tendency to push into the underlying musculature.

measures of the most conservative sort will usually suffice, such as radial cauterization of a chronic erosion of the cervix. It is when the lesion is so marked as to become really "suspicious" that biopsy has its great field.

It is easy to believe that epithelial lesions of this type, in which there is a more or less marked hyperplastic tendency already, would step across the line into actual malignancy more readily than do the epithelial cells of the normal cervix. Nor does it seem unnatural to



think that they might at times be caught in a transition stage, if such a transition really occurs. But as yet the evidence is strongly against such a view. For example, the growing margins of a cancer are usually sharply marked off from the normal tissue, from a histologic point of view at least. This is well shown in adenocarcinoma of the uterus, where the margin often shows the characteristic cancer glands immediately adjacent to perfectly normal glands (Fig. 11). The latter, instead of being lighted up by the approaching cancer flame, are destroyed by the cancer, which derives its destructive growth from some innate character of its own cells.

There can be little doubt that, in addition to such local lesions in the cervix, there must be present a constitutional predisposition of some unknown sort before cancer can develop. But to minimize the importance of the local factor because of this fact, as some would do, is highly illogical. Both the constitutional and the local factors are important. The first we can do nothing to control, because we know nothing of its nature. On the other hand, the predisposing rôle of chronic irritating lesions has been established beyond reasonable doubt, and the eradication of such lesions is usually easily possible. In fact, it is about all we can do along the lines of actual cancer prophylaxis. The physician who is on the alert for cancer in its early curable stage will find many lesions which are not cancerous but which are of this distinctly predisposing type. The correction of such lesions will confer at least a measure of safety upon the patients thus treated.

The time will undoubtedly come when the diagnosis can be made earlier and more precisely than at present. Efforts are already being made along this line, especially by the method of differential staining. For example, Schiller<sup>11</sup> has recently been advocating the use of Lugol's solution of iodine to the gross lesion for this purpose, on the ground that the cancer cell contains no glycogen, while the normal cell does. Already, however, the evidence against the reliability of this particular test is quite convincing, but the possibilities along this general line are definite. The use of Hinselmann's colposcope, by means of which lesions of the cervix or vagina are studied by illumination and magnification, may be of auxiliary importance in certain cases. That it can achieve a more important position seems to be doubtful from the reports available in the German literature, where it has been much discussed. For the present, therefore, the microscope must remain the court of final resort in the diagnosis of cancer. Even now, as I have indicated, the proportion of error is not disturbingly high, and even this proportion should be lessened by the knowledge derived from a more widespread study of the disease in its earlier stages.

#### SUMMARY

This paper deals with the matter of pathologic differentiation in lesions of the uterine cervix or body, which clinically are suspicious of

cancer, i.e., those cases in which biopsy or diagnostic curettage is usually called for. While cancer will rarely be found where there is no clinical suspicion whatever of its presence, it is revealed in a not inconsiderable proportion of cases which clinically are only suspicious. In an even larger proportion such lesions will be found to be benign, so that a patient will be spared the misfortune of the unnecessarily radical treatment which would be entailed by a policy of operating "on suspicion," or because of a belief that the suspicious lesion is precancerous. Most lesions which are precancerous, in the sense of predisposing to cancer, in themselves are easily curable by simple conservative measures.

In the cervix, especially, pseudomalignant pictures are extremely common, especially with chronic inflammations and polypi, but, with few exceptions, the microscope will clear up the diagnosis and point the way to the proper treatment. These pseudomalignant lesions are discussed in the paper, more especially as they bear upon the diagnosis of cancer. As cases come to the gynecologist earlier, there will be an increasing proportion in which the microscope will be essential for making rather than merely confirming the diagnosis of cancer. In doubtful cases involving the endometrium, representing chiefly cases of uterine bleeding in women beyond thirty-five where an obvious cause is not present, the microscope is essential in a much larger proportion of instances. Follow-up studies have shown the general trustworthiness of microscopic examinations after biopsy and diagnostic curettage, for the microscopic diagnosis, when made by a competent pathologist, is rarely belied by the operative findings or the subsequent course of the patient.

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LEUCOPLAKIC VULVITIS AND CANCER OF THE VULVA  
(ETIOLOGY, HISTOPATHOLOGY, TREATMENT,  
FIVE-YEAR RESULTS)

BY FRED J. TAUSSIG, M.D., ST. LOUIS, MO.

IT IS not often in the study of cancer that, with increasing years, we become more and more optimistic. Yet such has been my experience with cancer of the vulva, for while in 1912 in my first report of 8 cases, I gave a gloomy picture of this disease, an analysis of the present series justifies the conclusion that next to cancer of the uterine body it is the most benign type found in the female genitals, since approximately 50 per cent can be prevented, and, of those cancers that have already developed, about 60 per cent can be permanently cured. If we do not attain such results, I am convinced this is due largely to a failure to appreciate the predisposing factors in the disease and the proper treatment for its cure. Because of the relative infrequency of the disease, many surgeons and gynecologists have not taken pains to study the operative technic and cases have only too often been given slipshod treatment with disastrous final results.

This paper is based on the study of 40 cases of leucoplakic vulvitis and 76 cases of cancer of the vulva observed since 1907. They do not include the cases of primary cancer of the female urethra, although those instances where the cancer took its origin from the vestibular skin surrounding the meatus were classified as vulvar tumors. If the total number of these cases (116) seems large, this has been due in part to the generous cooperation of my colleagues, Drs. Gellhorn, Crossen, Ehrenfest and O. H. Schwarz, some of whose cases (26 in all) have been included in my studies; in part also to my special interest in this subject for the past twenty years, because of which a greater number of these patients have been referred to me. A majority of them were observed and operated upon at the Barnard Free Skin and Cancer Hospital.

This whole subject has been given but scanty consideration in recent literature and in the last ten years practically the only important contributions were those by Giesecke, 44 cases (1921); Sabre-Casas and Carranza, 37 cases (1928); and Graves and Smith 15 cases (1929). In former communications I have taken up the literature previous to 1920. Those interested will find in Graves a full review of the literature pertaining to leucoplakic vulvitis and kraurosis. Hence, I refrain from going into that phase and will proceed directly with a narration of my own experiences, referring from time to time to the work of others in discussing certain points.

In addition to the 40 cases of leucoplakic vulvitis, there were 39 vulval cancers in which a leucoplakic vulvitis was coexistent. In almost all of this latter group at the time of operation, the entire vulva was removed as well as the cancer, so that the leucoplakic lesions were available for microscopic study.

I regret that Graves has seen fit to retain the term kraurosis in preference to leucoplakic vulvitis. He agrees that the latter name is more accurate but says general usage makes him prefer the term kraurosis. This seems illogical. We might as well continue indefinitely to refer to all toxemias of pregnancy as eclampsia instead of limiting it to those that terminate in convulsions. In similar wise I

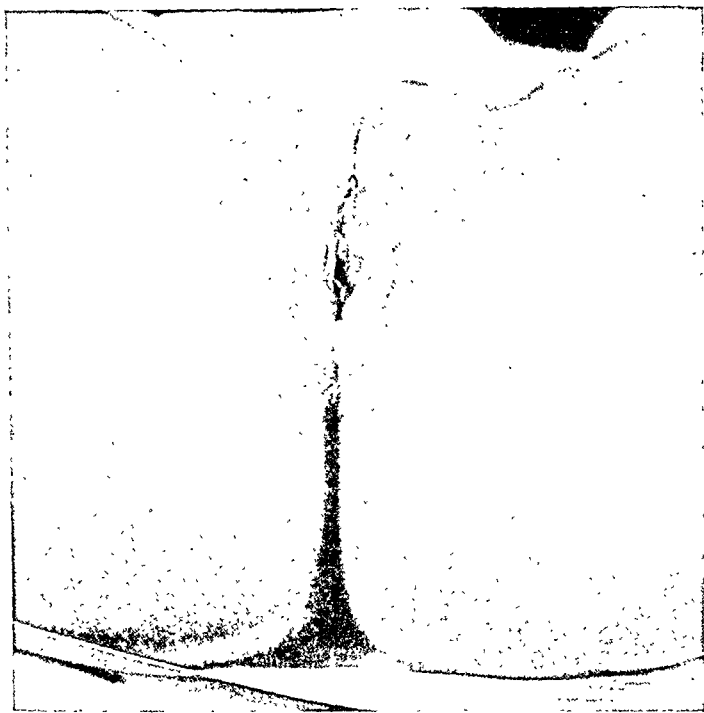


Fig. 1.—Leucoplakic vulvitis with kraurosis (early stage). The prepuce and perineum show leucoplakia while the labial region has the dusky red color known as "kraurosis rouge."

think we should limit kraurosis to those cases of leucoplakic vulvitis that terminate in obliteration of the labial and preputial folds.

#### LEUCOPLAKIC VULVITIS

The considerable majority of patients suffering from leucoplakic vulvitis have a symmetrical involvement of the entire nonhairy portion of the vulvar skin extending from the mons veneris to the margins of the anal ring. Occasionally the lesions are found to extend for a distance of 2 to 3 cm. around the anal ring. Of this generalized symmetrical type I found 28 out of 40 in my series. The lesions were not always found equally pronounced over this entire area. In fact it was the

rule that the leucoplakia was more definite in the preputial folds above and in the perineoanal region below, the itching sensation being more marked about the clitoris and the anal folds. In 6 of my series there was symmetrical localization of the disease over the perineum and around the anus without any lesions about the labial and preputial folds. In the remaining 6 cases the leucoplakia was over a smaller patch located asymmetrically and at times limited to only one side of the vulva.

The obliteration or flattening of the labial and preputial folds to produce the condition known as kraurosis was present in 22 of the cases but not in every instance was this kraurosis equally pronounced. At times a small ridge was present in the upper labia minora and prepuce, at times they were practically flush with the surrounding skin, leaving only a dimple in the region of the minute gland of the clitoris. To some degree the extent of the kraurosis was in direct proportion to

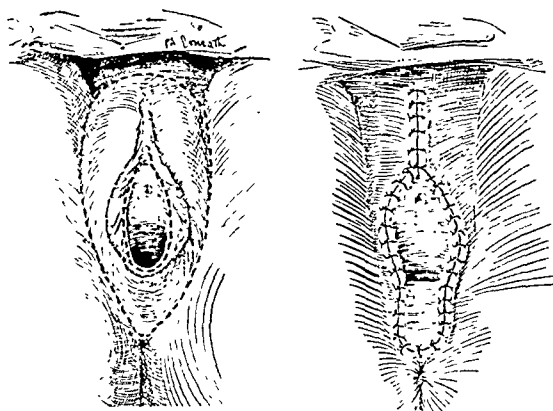


Fig. 2.

Fig. 3.

Figs. 2 and 3.—Vaginal flap operation for leucoplakic vulvitis. After removing the involved vulvar skin, the posterior vaginal wall is dissected free, and, after a cut into each lateral vaginal sulcus, the flap is drawn over the perineum and anchored to the anterior margin of the anus with interrupted stitches. (From Nelson's Looseleaf Surgery on Gynecology, pp. 678, 679.)

the severity and duration of the inflammatory process. Unfortunately only a small number of patients were observed within the first year or two of the disease. The majority had had symptoms for a long time before they finally made up their minds to seek medical advice. In these earlier cases the gross appearance was different. The leucoplakic areas were in spots or ridges over the prepuce or perineum or between the anal folds, while the remaining skin, though dry and flabby in tone had either a greyish-pink or dusky red color. In several of the early cases this dusky red mottling in the region of the labia minora to either side of the introitus vaginae was quite characteristic. Jayle, who made similar observations, called this lesion "kraurosis rouge." Even in this early stage, however, one notices the marked brittleness of the skin. Simple separation of the labia for inspection will often produce a superficial crack in the epidermis especially over the peri-

neum. In the more extensive and older lesions the entire skin assumes a thin parchment-like appearance with patches of greater thickness and whiteness and numerous superficial excoriations produced by the scratching.

From a racial standpoint it is of interest that the material for this report came largely from clinics where about 50 per cent of the clientele were colored women, yet only one case in this series of 40 was found in a negress. This patient had a large leucoderma over the upper vulva and it was at the edge of this leucoderma that there developed over the labium minus a small area of typical leucoplakic vulvitis. At this time it should be mentioned that in one case of carci-

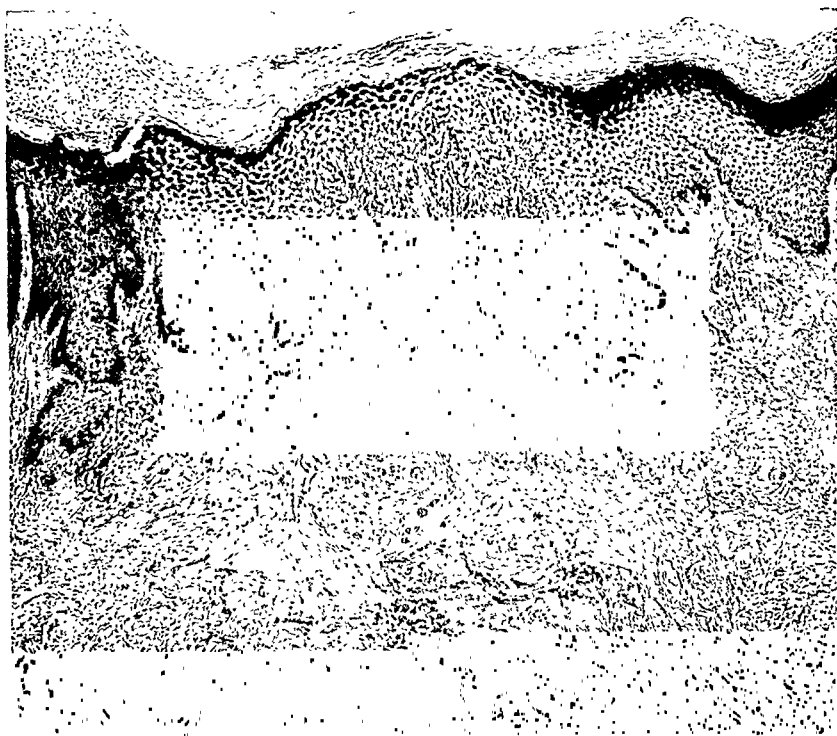


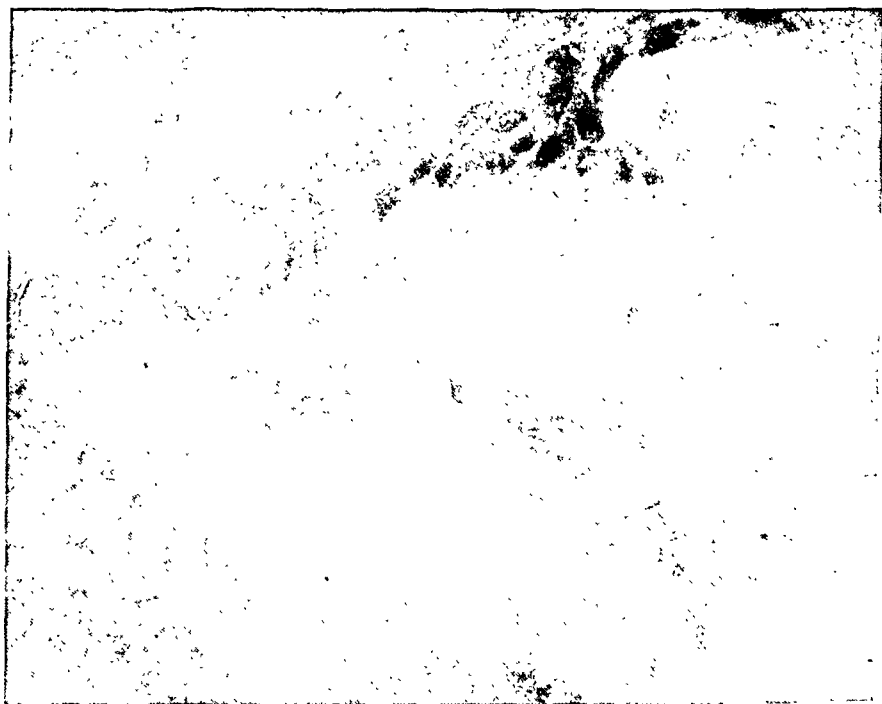
Fig. 4.—Leucoplakic vulvitis: hyperplastic stage. Note from above downward, first, the greatly thickened layer of keratin cells (hyperkeratosis); second, the increased number of eleidin cells, forming an almost black band; third, the granular zone sending long papillary processes of epithelium into the connective tissue (acanthosis); fourth, the connective tissue showing marked round cell infiltration, most marked directly beneath the epithelium.

noma of the vulva in a negress the disease developed upon a definite preputiolabial leucoplakia (see Fig. 9). From this it seems reasonable to assume that the greater elasticity of the negro skin, as witnessed by the rarity of perineal tears at childbirth, is a factor predisposing against the development of leucoplakic vulvitis in this race.

That leucoplakic vulvitis usually follows a cessation of ovarian function has been sufficiently emphasized in previous articles. In 30 out of the 40 patients in my present report this was the case. The average age of the patients was forty-nine years, the oldest one being seventy-



A.



B.

Fig. 5.—Leucoplakic vulvitis. A stage midway between the hyperplastic and atrophic condition: (A) low power field, showing a zone of pigmented hyperkeratosis, eleidin layer still marked, epithelial layer sending short processes downward, and beginning development of collagenous areas in the connective tissue directly beneath the epithelium; (B) high power of area outlined in (A) showing collagen formation in the connective tissue.

four and the youngest twenty-six. Of the 10 patients who had not yet reached the menopause, some abnormality of menstrual function was noted in all, although this was not always pronounced. One of the

most interesting in this regard I had occasion to observe only a few months ago. She was a young married woman of twenty-six years, who stated that ever since the onset of menstruation at the age of fourteen, she had suffered from a pruritus of the vulva, that became increasingly severe with each year. Although married for over a year sexual intercourse had been impossible owing to a kraurosis of the vaginal introitus resulting from this leucoplakic vulvitis. Microscopic examination of the vulval tissues after vulvectomy in this case showed the typical lesions found in this disease.

Sterility is not in any special way associated with the disease. Where such a vulvitis occurred after the menopause, it was found as often in women who had had many children as in those who had had none. In one woman pregnancy occurred for the first time after removal of the leucoplakic vulva. In another the lesions were seen for the first time coincident with a pregnancy.

Pruritus of long standing is the almost unfailing symptom of leucoplakic vulvitis. There were but one or two exceptions to this rule and in them the lesions were still very slight and the patients stated that the vulval skin in this region felt dry and sore. The duration of the pruritus before treatment was carefully noted in 27 patients and averaged over five years. In seven instances it had lasted from ten to fifteen years before the patient came under our observation. So intense was the pruritus that many of the patients were "nervous wrecks," suffering from insomnia, for it was the invariable rule that the pruritus was more severe at nighttime.

Burning after urination was present if there was marked excoriation of the vulva. Pain on defecation was noted if the anal lesions were pronounced. A not inconsiderable number had a pronounced vaginal discharge, which added to the chafing of the vulval skin. In many of the patients with kraurosis, dyspareunia was so marked that sexual intercourse was no longer attempted.

The clinical course of the disease is usually a slowly progressing one, although in some instances there are long periods where the process remains stationary or diminishes in severity. It is difficult in view of the rarity of both leucoplakic vulvitis and cancer of the vulva to follow any appreciable number from the stage of leucoplakia to that of malignant change or to determine accurately the percentage of this form of vulvitis that eventually becomes malignant. If however over a certain period of time I have had occasion to see 40 cases of leucoplakic vulvitis without carcinoma and 39 cases of leucoplakic vulvitis with carcinoma, I think it can be assumed that in the course of the disease, eventually at least one-half will undergo a malignant change. As to a stage of complete healing of leucoplakic vulvitis described by Berkeley and Bonney I have seen many temporary alleviations but



I know of no five-year cures, spontaneous, medical or radiotherapeutic. For a short time the vulvar skin may look fairly normal but apparently the underlying pathology sooner or later starts off the process anew, and final relief is secured only by a complete vulvectomy.

*Treatment.*—An analysis of the treatment given these 40 patients shows that 25 were subjected to a more or less complete vulvectomy depending on the location and extent of the vulvitis. Some of the remainder refused further treatment when operation was suggested, or were given antipruritic salves and lotions. In 3 patients radium was used and in 3, x-ray therapy, but none of these six patients were more

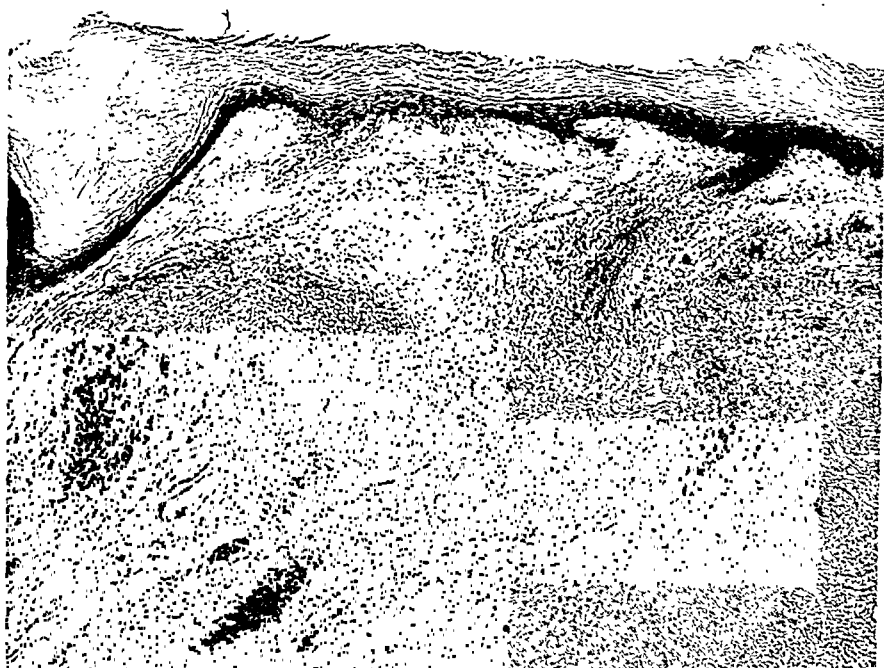


Fig. 6.—Leucoplakic vulvitis; atrophic stage. Here we see an area of pronounced hyperkeratosis, beneath which is a greatly thinned strip of epithelium, 3 to 4 layers, with few eleidin cells, an irregular, frayed out basement membrane, and only here and there a few short projections of epithelium into the subjacent connective tissue. The connective tissue shows large areas of collagenous deposit with zones of pronounced round cell infiltration. In some instances the sclerosis is more marked with less evidence of inflammatory changes.

than temporarily relieved by this procedure. The radium cases, although only gamma irradiation was employed, showed a prolonged radium reaction with superficial radium ulcer (average dosage 500 mg. hr.). The results of irradiation in any form were certainly very discouraging, although other observers seem occasionally to have met with success. Four of the 6 patients in my series were subsequently subjected to a vulvectomy. The use of corpus luteum and ovarian extracts was equally unsatisfactory. Occasionally a patient would seem to be temporarily relieved. One patient reported after a five-year period that

by the regular use of vaginal antiseptic douches the pruritus was completely relieved and while the skin still showed definite leucoplakic changes, she was symptomatically well.

A special effort was made to follow up the patients over a period of years. Of the 23 vulvectomies, 4 were lost track of; 2 died, one died on the fourteenth postoperative day of coronary embolus, and the other died within a year following operation of tabes dorsalis. Of the remaining 17 patients, 16 were cured, 9 of them for periods longer than five years. These patients were all personally reexamined by me. Two

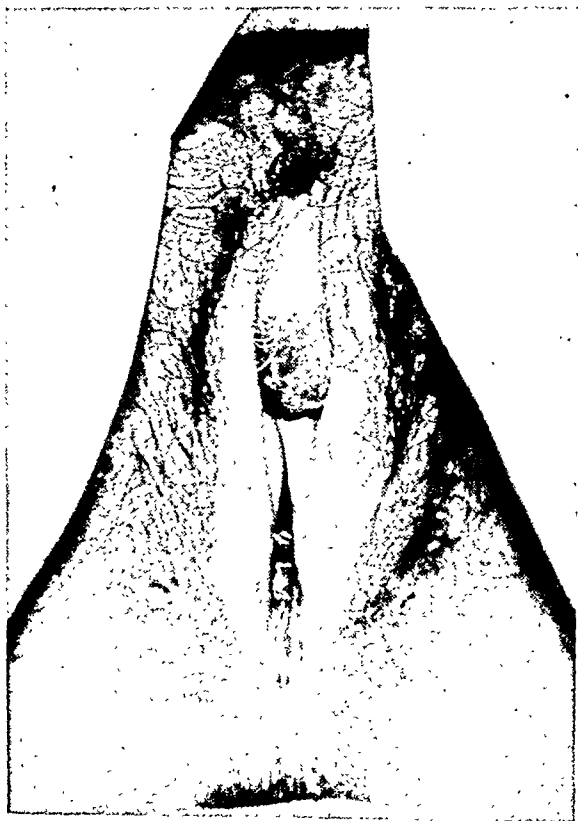


Fig. 7.—Carcinoma of the prepuce of the clitoris, an everting cauliflower nodule developing from the parchment-like leucoplakic vulvitis involving both labia, prepuce and perineum.

patients showed a small patch of keratosis near the anal margin, appearing in one, six years, in the other, eleven years after vulvectomy. These patches were less than 5 mm. in diameter and were easily and permanently removed by electrocauterization. One patient with a more extensive recurrence over the perineum two years after vulvectomy will require a second operation. The final result of vulvectomy may therefore be described as entirely satisfactory.

The relief from the tantalizing pruritus by means of vulvectomy is most striking. Even in the first few days the pain of the sutures and wound seems light compared to the suffering and insomnia produced

by the pruritus. In my earlier operative experience I had much difficulty in obtaining good wound healing. Particularly over the perineum, sutures would cut through and a large area heal by granulation with a stiff rigid scar. Another complication was the painful stenosis of the anus that often followed a complete removal of the perianal skin. To overcome these difficulties I have devised a modification of the usual technic of vulvectomy as follows:

*Vaginal Flap Operation.*—After removing the entire nonhairy portion of the vulva from the mons veneris to the anterior anal margin, including the prepuce, clitoris, labia minora, inner aspect of labia majora, and perineal skin, all bleeding points are caught and ligated. Then the posterior vaginal wall is dissected free from the rectum and levator muscles, as in a perineorrhaphy, for a distance of about 6 to 7 cm.



Fig. 8.—Early inverting carcinoma of the right labium, springing from an asymmetrical leucoplakia of the upper vulva. Epidermal type.

upward. A cut 3 cm. along each vaginal sulcus will now mobilize this flap and permit it to be drawn outward over the perineum so that it can be sutured to the anterior margin of the anal ring (Fig. 2). In this way it fills in the gap between vagina and anus, which it is usually difficult to cover by the neighboring skin without tension and without producing a painful cicatrix at the entrance of the vagina. I have now done this type of plastic closure of a vulvectomy in 6 cases of leucoplakic vulvitis with uniformly satisfactory results. In only one instance was there a partial slough along one edge of the vaginal flap.

*Double Anal-Bridge Operation.*—To overcome the tendency for the anal mucosa to break loose and retract where it is tacked directly to the

outside skin after extensive circular removal of the perianal leucoplakic skin, I have in my last case of this kind left intact a bridge of anal skin on either side, about  $1\frac{1}{2}$  cm. in width. Even though a small patch of leucoplakia may be present on such an anal bridge, the cutting off of the tributary nerve supply prevents a return of the pruritus. By thus keeping a grasp on the anal mucosa on either side, we can proceed above and below with fairly extensive removal of the affected skin without danger of producing a stenosis and extensive and painful scar-tissue formation around the anus. This complication of painful anal strictures has been one of the most annoying complications of the complete vulvectomy in the past, and the results obtained in this first case justify the feeling that the use of the double anal bridge will greatly improve the postoperative course in these cases.



Fig. 9.—Leucoplakic vulvitis in a negress involving labia minora, prepuce and adjacent skin with a beginning carcinoma of the right prepuce at point marked x.

*Histopathology.*—Material for histologic study was obtained in 25 of the cases of uncomplicated leucoplakic vulvitis, and in 39 of the cases in which it was found in combination with carcinoma of the vulva. In almost every instance sections were made from 4 or 5 different blocks, so that the present conclusions are based on a study of over 500 sections made in 64 cases. Naturally there was considerable variation in the nature and extent of the lesions found and even in the same case there was often a decided difference between sections taken from various portions of the affected skin. In general, however, I have found little to change the observations as stated in previous publications. The most important variation is in the direction of greater simplicity, for instead of dividing the condition into three or four stages as was

done before, I think it more logical to divide this condition simply into an early hyperplastic stage and a late atrophic stage.

In the early stage we find extensive subepithelial leucocytic infiltration with pronounced elongation of the epithelial papillae (acanthosis) and beginning thickening of the keratin layer. In the beginning, nuclear elements are still present to some degree in this keratin layer and the term parakeratosis has been applied to this stage in distinction from the later hyperkeratosis where only thickly packed keratin fibers are found. In the course of a few months or a year if the pruritus has been pronounced there is noted a marked increase in the thickness of the eleidin layer and in the quantity of eleidin deposited in these cells. Since this substance stains very deeply with hematoxylin this layer often appears as a thick black band beneath the keratin. The epi-



Fig. 10.—Multiple carcinoma of the vulva on a basis of leucoplakic vulvitis. Where an incomplete vulvectomy is done in cancer on a leucoplakic basis, a new cancer may spring from the remaining area of leucoplakia. Three instances of this sort occurred in my series. The lymph glands in the case photographed above showed carcinoma (Fig. 17). Patient is free of recurrence five and a half years since operation.

thelial layer in this early hyperplastic stage is as a rule from 4 to 6 times thicker than in the normal individual. In the connective tissue there is considerable hyperemia and marked round cell infiltration. Only toward the conclusion of this stage do we notice increasing connective tissue formation with some sclerosis.

The late atrophic stage is not an abrupt change. There are gradations between it and the hyperplastic stage so that areas midway between the two are commonly found. Yet the lesions of this late stage are so characteristic and different from the early stage that it seems histologically almost like two diseases. As we approach the late stage we observe increasing hyperkeratosis, pronounced eleidin but lessened

acanthosis. The papillae become much flatter and shorter, even though the total thickness of the epithelial layer is still twice that of the normal. There is also diminished round cell infiltration and increasing sclerosis of the dermis.

The typical late atrophic stage is a very distinctive picture. It is the one described by Breisky and found almost invariably in those cases with obliterated labial and preputial folds (kraurosis). Since it is however also found just as pronouncedly in lesions located in the perineal and anal regions, without any general vulval flattening, we



Fig. 11.—Carcinoma of the vulva springing from the left upper edge of a syphilitic tertiary ulcer. Vestibular type.

cannot call this stage, as Graves does, kraurosis. The epithelial layer in these cases consists of a considerable layer of hyperkeratosis, beneath which is found a thin layer of eleidin cells, and then, with papillae absent, a flat strip of pavement cells that may or may not be covered by a single layer of basement epithelium. In many areas the border of this pavement epithelium appears frayed out and irregular without any sharp distinction from the connective tissue beneath. Even more marked are the changes in the dermis. The round cell infiltration is in more or less circumscribed lymph zones, much less marked than in

the early cases, with plentiful plasma and mast cells scattered through the connective tissue. This connective tissue in many areas directly beneath the epithelial layer undergoes a peculiar collagenous change, forming patches of glairy tissue containing only a few normal cells.

I have left to the last a description of the elastic tissue in this disease since it has rightly been emphasized in all descriptions as of great significance. Even in the earliest lesions examined\* I never failed to note some diminution in the amount of elastic tissue between the epithelial papillae of the skin and directly beneath the basement membrane; this absence of elastic fibers became increasingly marked as



Fig. 12.—Carcinoma of the vulva developing on a tertiary gumma with hypertrophic vulvitis in a negress.

the disease advanced and was most pronounced in the late atrophic stage of the disease. There was complete absence of these fibers in the upper dermal zone, but directly beneath this area where you first noted the elastic tissue, it was piled up like kindling wood in irregular pieces and strips, so that you had the impression not of absent, but rather of dislodged, disintegrated, elastic fibers.

A study of the 39 cases in which carcinoma was implanted on a leucoplakic base revealed histologically that in 60 per cent the malignant changes took place in an early hyperplastic area and in 40 per

\*In three private patients under previous treatment for other conditions, the leucoplakic vulvitis was noted within a few months of its onset.

cent in a late atrophic area. Hence carcinoma may develop at either stage of the disease, although it is a little more prone to spring from the hyperplastic lesions.

*Conclusions.*—From the clinical and pathologic evidence of leucoplakic vulvitis thus far obtained, I think it reasonable to assume that in certain individuals as a result of an alteration or cessation of ovarian hormones there occur changes in the elasticity of the skin which lead to increased friability of the epithelial covering. In the presence of a vaginal discharge or even without it, minute multiple subepithelial infections occur, which by swelling of the neighboring



Fig. 13.—Carcinoma of the glans clitoridis. Note the absence of leucoplakia and the subdermal development of the tumor.

tissues produce a feeling of itching. This pruritus in turn leads by scratching to increased traumatism of the affected skin and so a vicious circle is started that results first in a chronic infection, then in epithelial hyperplasias and finally in certain sclerotic atrophic changes.

#### CARCINOMA OF THE VULVA

Only about one out of every 20 or 25 cancers in the female genital tract arise from the vulva. If the proportion was relatively greater in my series, it was probably because my material came largely from a skin and cancer hospital, to which skin cancers of all sorts were widely referred. The average age of my patients was fifty-nine in vulval



cancer in contrast to forty-nine in leucoplakic vulvitis. The youngest patient in my series was twenty-six years of age and the oldest one eighty-seven years. Only 3 patients out of 76 were colored women, a relatively small proportion and in 2 out of these 3 the carcinoma developed not from a skin lesion but from the edge of an old syphilitic ulcer at the fourchet.

*Anatomical Forms.*—Carcinoma of the vulva is by no means a single disease, for upon closer study we find that there are four definite and distinct forms, varying decidedly in accordance with the point of origin of the tumor. This point has I believe not heretofore been stressed as it should have been. These four forms are:

1. Epidermal
2. Clitoris
3. Vestibular
4. Bartholin gland

1. The *epidermal* form is by far the most frequent. Out of the 67 cases of my series in which a fairly definite classification could be made, 51 sprang from the labial, perineal, or preputial skin. Only in the very early cases could a differentiation between labial and preputial origin be made, but the fact that in 9 instances the onset was clearly in the region of the prepuce speaks for the relative frequency of this type. In the past this preputial cancer has been wrongly classified as carcinoma of the clitoris. It resembles closely in etiology, spread and histologic structure the form found immediately adjacent in the labial skin. Let us not forget that the prepuce is anatomically merely an extension of the labial folds. Etiologically this epidermal cancer springs from leucoplakic vulvitis in almost every instance. Occasionally warts or traumatic scars may be a factor.

2. True carcinoma of the *clitoris* is a very rare and interesting disease. As seen in Figs. 13 and 14 the cancer begins beneath the surface of the skin in the epithelium of the glans itself. Histologically it presents a very different picture. The cells are smaller and more rounded and the nests are more loosely formed so that in areas there is a resemblance to sarcoma. Apparently this is a very malignant tumor for the cells are of undifferentiated embryonal type, and there are very numerous mitoses. Only two of the cases in my series were of this clitoris type and neither of them were associated with leucoplakia of the neighboring skin. The etiology of these tumors is unexplained.

3. *Vestibular* carcinoma was present in 10 cases in my series. The vestibular epithelium resembles more closely that found in the vagina than that of the epidermis. The type of carcinoma that springs from it also has distinguishing characteristics. It forms superficial indurated ulcers. Those situated near the urinary meatus are relatively

benign, but those that originate around the vaginal orifice tend to invade the vagina and then assume all the malignancy of a vaginal cancer. Eight of the 10 vestibular cancers in my series developed at the edge of an old syphilitic ulcer. From this it would appear that the etiologic association of syphilis in this type is just as definite as is that of leucoplakic vulvitis in the epidermal type. Histologically and clinically these cancers are malignant, they show nests of medullary undifferentiated epithelium with many mitoses.

4. *Bartholin gland* cancer has been long recognized as a special type. It may be either squamous or adenocarcinomatous but always begins as a subepidermal tumor as shown in Fig. 16. There were 4 Bartholin gland tumors in my series. In 3 of these a definite history of a pre-



Fig. 14.—Carcinoma of the glans clitoridis with perforating ulcer but no involvement of the prepuce or labia.

vious Bartholin gland infection was obtained; once the gland had been incised. The tumor, because of its location beneath the epithelium, reaches a considerable size before it causes enough discomfort to compel the patient to seek medical advice. Hence, fewer of these cases are cured.

The lymphatic spread of all 4 types of vulval cancer is similar: at first to the superficial inguinal and femoral, then to the glands just beyond the inguinal canal and those internal to the femoral ring, finally to the iliac and aortic lymph glands.

The subject of the etiology of vulval carcinoma has been treated at length in my previous publications. Without giving at this point the clinical and histologic evidence on which this diagnosis of etiology is

based, I can say that an analysis of my cases shows the following distribution:

Leucoplakic vulvitis	39 cases
Syphilis (tertiary ulcers)	8 cases
Condyloma acuminata senilis	2 cases
Chronic bartholinitis	3 cases
Trauma	3 cases
Uncertain	21 cases

I was greatly interested in the study made by Smith in his joint publication with Graves. He found in an examination of 21 specimens of vulval carcinoma in his laboratory that 16 showed leucoplakic changes. This would make a ratio of 75 per cent of cancers due to

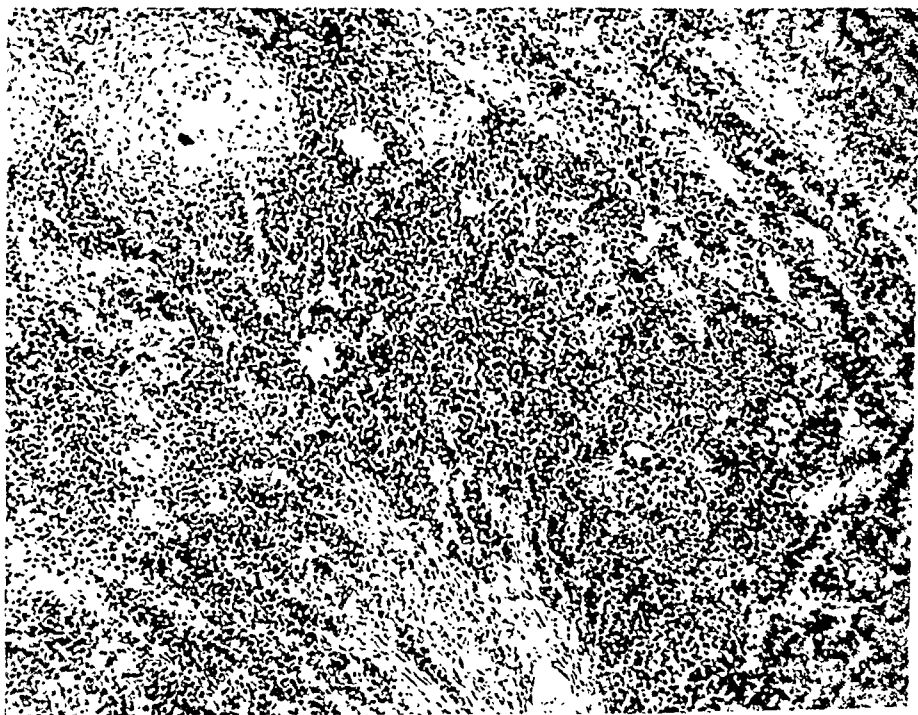


Fig. 15.—Carcinoma of the glans clitoridis. Microscopic section taken from case shown in Fig. 13. Note the sarcoma-like character of these tumors. They are very malignant (Malignancy index Type 4).

leucoplakic vulvitis. While in my series the percentage definitely due to leucoplakia is only a fraction over 50 per cent it should be remembered that Smith is dealing only with specimens from operable cases while I have included every vulval cancer that came under observation even though inoperable. If I had taken only the 49 cases in which a vulvectomy was done, it would have shown 39 cases of leucoplakia or about 80 per cent. These figures correspond closely to Smith's and indicate the greater operability of those cancers that develop on a leucoplakic basis.

The development of cancer of the vulva on a syphilitic basis has been carefully described by Dr. Gellhorn, including several cases in

this series. Fig. 11 is an excellent instance of a very early lesion developing on the upper edge of a typical tertiary ulcer. The interesting clinical fact of this group of 8 cases is the relatively high percentage of negroes, and the development of the carcinoma at an average age of thirty-eight in contrast to an average of sixty-four years for those cases where the cancer developed from a leucoplakic vulvitis.

The symptoms and course of carcinoma of the vulva need no special amplification. Pruritus was present in practically all cases preceded by leucoplakia. The ulcer produced a feeling of soreness with burning in the wound after urination. Bloody discharge was present but very



Fig. 16.—Carcinoma of Bartholin's gland. A history of previous Bartholin infection was here recorded. Note subdermal development.

rarely any extensive bleeding; pain in the more advanced cases radiating down the legs with an increasing edema of the legs as the disease advanced; relatively early metastases to the tributary inguinal and femoral glands and relatively late metastases to more distant glands and organs.

Although there is always some artificiality in any method of dividing cancers into groups according to the amount of involvement, I have attempted to do this for carcinoma of the vulva in the following way:

Group I. Cases without palpable metastasis, tumor 1 to 3 cm. in average diameter.

Group II. Cases without palpable metastasis, tumor 4 to 7 cm. in average diameter.

Group III. Cases with ulcer over 7 cm. in average diameter or deeper infiltration or palpable gland metastasis.

Group IV. Large ulcer with vaginal involvement or large cancerous lymph glands.

Group V. Far advanced tumors with broken down lymph glands and cachexia.

All cases in Groups I and II and most cases in Group III would be classified as operable; the remainder as inoperable. In my series there were found: Group I, 17 cases; Group II, 17 cases; Group III, 19 cases; Group IV, 16 cases; Group V, 7 cases. This would point to an operability of about 60 per cent. However 4 of the cases in Group I and II refused operation and in another patient the extreme age, eighty-seven years, made any such procedure seem inadvisable.

*Malignancy Index.*—The interesting and valuable observations regarding the malignancy index in cancer of the cervix made by Martzloff, Schmidt, Healy and others, led me to go over all my material with this in view to determine the value of a malignancy index in cancer of the vulva. Out of 76 cases in my series, the lesions were far advanced in 12 and no tissue was removed for diagnosis. In 6 cases tissue was removed for diagnosis but the sections were for some reason not available or suitable for the purposes of this examination. There remained then 58 cases that could be studied. In practically every instance a large portion of the tumor or the entire vulva was available for study and sections were made from various areas. I have tried to follow Broders' idea in dividing the cases into 4 types in accordance with the amount of anaplasia. Special attention was paid to cellular overgrowth, variation in size, shape, and staining qualities of the cells and their nuclei, infiltration tendencies, number and character of mitoses, connective tissue reaction. Dr. Jorstad, pathologist of the Barnard Free Skin and Cancer Hospital, checked my findings and was in agreement in practically every case.

Of Type 1, in which the cells were well differentiated with large areas of well formed pavement epithelium and large areas of pearls and but very few atypical cells or mitoses, there were found 7 cases.

Of Type 2, in which there was also well-developed pavement epithelium with occasional pearls but with a definite rim of atypical, deeply staining cells showing more numerous mitoses, there were 30 cases.

Of Type 3, in which the cells were grouped in medullary nests with only occasional small areas of a pavement-type cell, with plentiful mitoses, there were 16 cases.

Of Type 4, in which the structure of the tumor was loose, the cells spindle-shaped or markedly polymorphous, with giant cells, and countless mitoses, there were 5 cases.

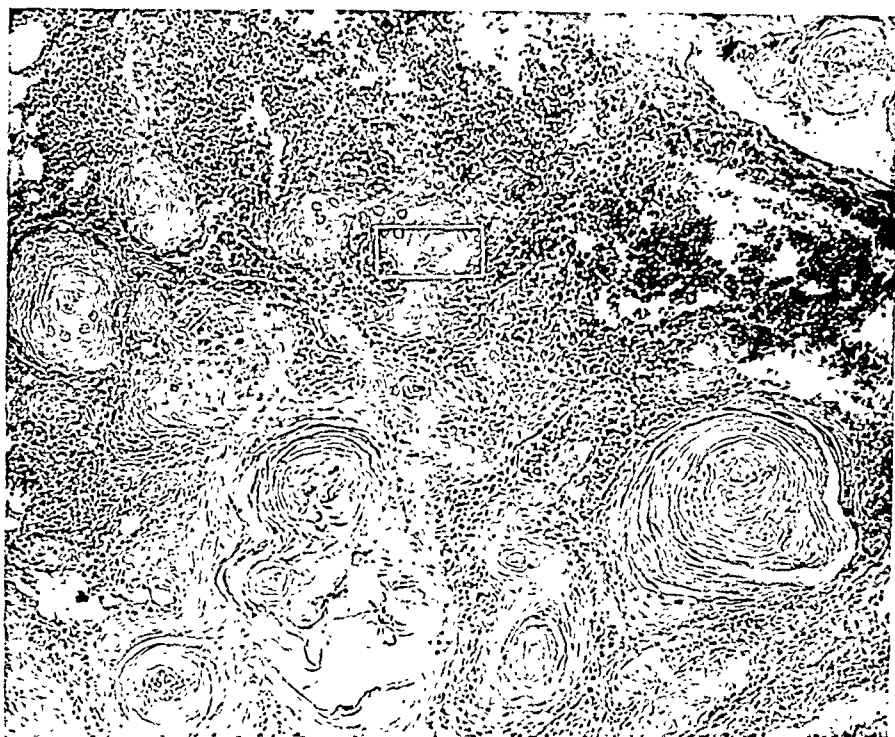
The relationship of this malignancy index to the amount of involvement proved rather interesting and may in a sense be regarded as evidence of the value of such a histologic classification. The findings were as follows:

Group I (Ulcers 1 to 3 cm.) showed	Type 1 = 5 Type 2 = 8	} average 1.61
Group II (Ulcer 4 to 7 cm.) showed	Type 1 = 2 Type 2 = 9 Type 3 = 2 Type 4 = 2	} average 2.26
Group III (Infiltrating ulcers) showed	Type 2 = 7 Type 3 = 8	} average 2.53
Group IV (Large ulcers with carcinoma in glands) showed	Type 2 = 4 Type 3 = 4 Type 4 = 2	} average 2.80
Group V (Large tumors, necrosis, cachexia) showed	Type 2 = 2 Type 3 = 2 Type 4 = 1	} average 2.80

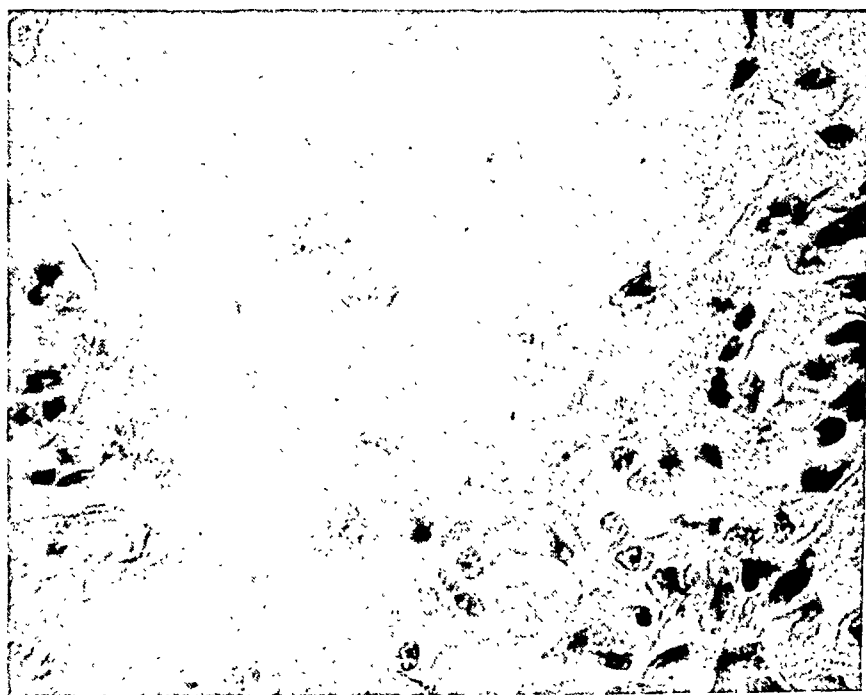
Thus we see that the cases that spread most rapidly and extensively showed the highest malignancy index. It is of special interest that the malignancy index in the epidermal cancers was much lower than was the case in the vestibular, clitoris or Bartholin gland tumors. Especially the cases that developed on a syphilitic basis in younger persons and those originating in the glans clitoridis showed a high malignancy index.

*Treatment.*—It is not surprising in view of the extreme age of some of these cancer patients that all treatment is at times refused. Six of our 76 patients were either untreated or else referred back to their family physicians for palliative measures. Of the remainder 21 were given some form of radiotherapy (radium or x-ray or both), and the other 49 were subjected to some form of surgical operation, either a partial or complete vulvectomy (15 cases), a vulvectomy combined with superficial or incomplete gland removal (18 cases) or a vulvectomy with double-sided complete Basset removal of glands (16 cases).

*Radiotherapy.*—With increasing experience I have become more and more discouraged at the results of radiotherapy in these cases. I believe that any dosage sufficient to cause even a temporary retrogression of the tumor is very apt to produce a radium burn. Such burns about the vulva may appear many months after the irradiation. They are always excruciatingly painful and slow to heal. I have been repeatedly amazed at the hypersensitiveness of the vulval skin to such rays. The practically uniform failure of either x-ray or radium to produce even a temporary alleviation of symptoms or appreciable diminution in the size of the tumor leads me to the conclusion that radiotherapy is not only of no avail but that it is as a rule actually contraindicated. It seems to stir things up and lead to more rapid metastases. The only exception I would make is in the use of radon gold seeds implanted into the primary tumor, where surgery for some reason is refused or contraindicated. Bailey's immediate results were rather encouraging. I had one similar local retrogression for one and one-half years after



A.



B.

Fig. 17.—(A) Lymph-gland metastasis from case of vulval carcinoma depicted in Fig. 10. Malignancy index in this case was Type 1. (B) High power microphotograph of area outlined in Fig. 17-A, showing high degree of differentiation into pavement epithelium.

radon gold seeds, but of course the tributary glands in this case became enlarged and then had to be removed surgically. In 3 cases where radium was implanted as needles or seeds into cancerous lymph glands no benefit was noted. Sobre-casas, Giesecke, and others have had equally discouraging results with radiotherapy. Only from the Radium-hemmet of Stockholm come more encouraging reports, but here the radiotherapeutic measures were used in combination with the destruction of the tumor by electrocoagulation (diathermy). I have the impression that it is the diathermy that is largely responsible for whatever benefit the treatment may have produced. Even so, only 8 out of the 26 cases treated between 1922 and 1924 were symptomatically well and only one case for as long as three years. The fact that in this report the statement is made that operations for carcinoma of the vulva are almost always hopeless indicates sufficiently the rather warped point of view on this subject by the writers.

*Surgery.*—In the period between 1906 to 1915 relatively few cases were seen, and these were operated upon either by simple vulvectomy or by a removal of the superficial femoral and inguinal glands in combination with the vulvectomy. If in the cases since 1915 there was no fixed rule regarding the operative technic, this was due in part to the fact that the other surgeons in charge of the cases were not convinced of the necessity of such a radical double-sided gland dissection and in part to contraindications in the physical condition of the patient to extensive operative measures. In 3 patients adhesions between a cancerous lymph gland and the sheath of the femoral vessel made it impossible to complete the Basset type of gland removal. In a few instances the glands were removed only on the side where the cancer developed. All in all there were no serious operative difficulties, although great care had to be exercised when working close to the femoral and external iliac vessels. There were 2 postoperative deaths, one occurring twenty-four hours after a simple vulvectomy and the other occurring eight days after an operation in which the superficial removal of glands with vulvectomy was done. There were no operative deaths among the 16 patients on whom a double-sided Basset operation and vulvectomy were done. I think this favorable outcome is largely due to the fact that all the work was extraabdominal. Stoeckel and E. Kehrler have described a very extensive operation for gland removal in which they excised by laparotomy the iliac and hypogastric glands as well as the deep and superficial inguinal and femoral. Giesecke in his report from the Kiel clinic states that of the 15 cases where this technic was employed, 3 died from the operation (20 per cent). This is in my opinion too large a primary mortality to justify the procedure. I have hence retained the Basset technic especially as my five-year results are so very satisfactory.



The duration of the complete operation is often over two hours so that I have previously urged that it be done in two stages: one, the complete gland removal, and the other, the vulvectomy. Theoretically the gland removal should be done first and then the vulvectomy two weeks later, but where a large infected ulcer was present I have often found it more practical to clean up the vulva by a cautery excision first, proceeding with the Basset gland removal at a later time.

Regarding the technic of the vulvectomy, I wish only to stress the necessity of a complete removal of the leucoplakic skin to prevent the development of a new cancer and to warn against too radical an excision of the urethra where the cancer approaches this organ. The incontinence of urine where the urethra is removed is so distressing a

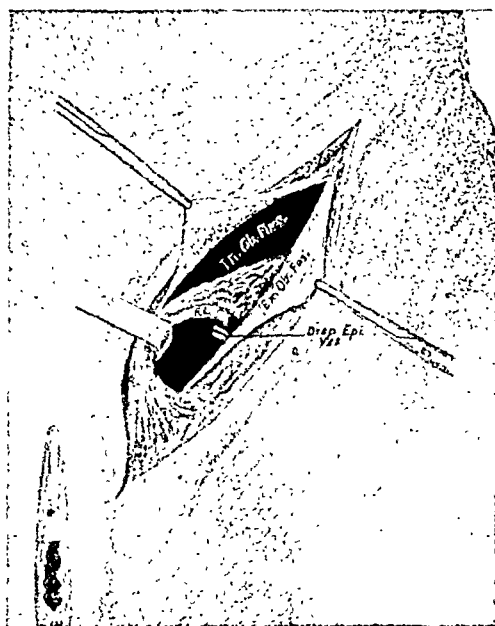


Fig. 18.—Basset's operation for lymph gland resection in carcinoma of the vulva (step 1). Incision over inguinal canal. Canal opened and round ligament isolated and lifted up. *R.L.*, round ligament; *Ex. Ob. Mus.*, external oblique muscle; *Ex. Ob. Fas.*, external oblique fascia; *Deep Epi. Ves.*, deep epigastric vessels.

complication that I would prefer to handle the urethral involvement in great part by the use of radium, since the urethra is very tolerant of radiation therapy.

The necessity of the removal of all the leucoplakic area is clearly demonstrated by the simultaneous appearance of multiple foci of cancer upon the vulval skin. Several cases of this sort were found in my series (Fig. 10). Even more is this shown by 3 cases in which a second new cancer developed some years later in another part of the vulva from a patch of leucoplakia that had not been removed. A brief record of these cases follows:

1. Ki. (Barnard, 492), sixty years, had a carcinoma of the left labium minus removed elsewhere by incomplete vulvectomy in 1913. In July, 1914, patient re-

turned with pronounced leucoplakic vulvitis over the right labia and entire perineum. At one point in the perineum a hard ulcer 1 by 2 cm. in diameter was noted that proved to be a new carcinoma.

2. G. (Barnard, 22009), thirty-nine years, had a small carcinoma of the upper left labia which was removed in combination with a double-sided Basset operation Sept. 23, 1920. At this time the entire labia were removed but the perineal skin did not appear involved in the leucoplakia and was not completely excised. On Sept. 12, 1923, an area of leucoplakia near the upper anal margin was noted in the center of which appeared an indurated ulcer 1 cm. in diameter. This was extensively excised with the surrounding deeper structure and proved to be a carcinoma. There has been no recurrence since that time. The last examination was made Jan. 30, 1929 (five and one-half years since the second operation).

3. Mrs. M. (Barnard, 22502), sixty years, had a carcinoma of the right labium majus, which was removed by vulvectomy and Basset gland removal, Nov. 24,

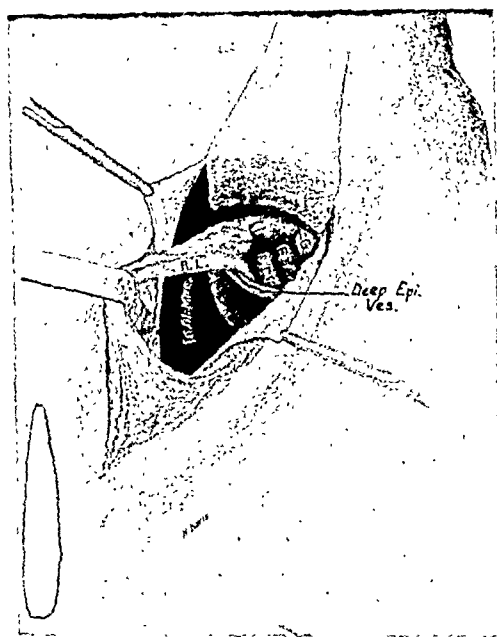


Fig. 19.—Basset's operation (step 2). Muscle retracted to expose internal iliac vessels and lymph glands to either side in iliac fossa. *G.*, gland; *E.I.A.*, external iliac artery; *E.I.V.*, external iliac vein; *R.L.*, round ligament; *Ex. Ob. Mus.*, external oblique muscle; *Deep Epi. Ves.*, deep epigastric vessels.

1920. No recurrence for over seven years. August 10, 1928, there was noted an area of leucoplakia, 1 cm. in diameter to the right of the urinary meatus, from which sprang a small papillary growth, that proved on section to be a carcinoma. Local excision. Patient died of influenza-pneumonia Dec. 8, 1928.

Cases of this kind have been noticed by others. H. R. Schmidt had two patients in whom over a period of from seven to eleven years new carcinomas developed on a leucoplakic basis at points far distant from the original tumor. It is important therefore in our operative procedures to remove all the leucoplakic skin and to consider any islands of leucoplakia that may subsequently become more prominent as potentially cancerous, removing them either by excision or cautery destruction.

*Basset Technic.*—Since the technic for removal of the tributary lymphatics described by Basset has proved so satisfactory as far as immediate and five-year results are concerned and since it has as yet not gained the recognition it deserves in the clinics of this country, a brief repetition of the important steps is in order.

1. An incision extending from a point 2 cm. internal to the anterior superior spine of the ilium, downward and inward, parallel to the inguinal canal, to 2 cm. below the tubercle of the pubis.

2. After pushing aside the skin and subcutaneous tissue, the aponeurosis of the external oblique muscle is incised parallel to the inguinal canal. The round ligament is thereby laid bare and then exposed along its entire course up to the inguinal ring. The peritoneum is pushed backward from the round ligament and the muscles of the abdominal wall retracted upward. In so doing, the lymph glands lying in the iliac fossa at either side of the external iliac vessels are exposed and can be

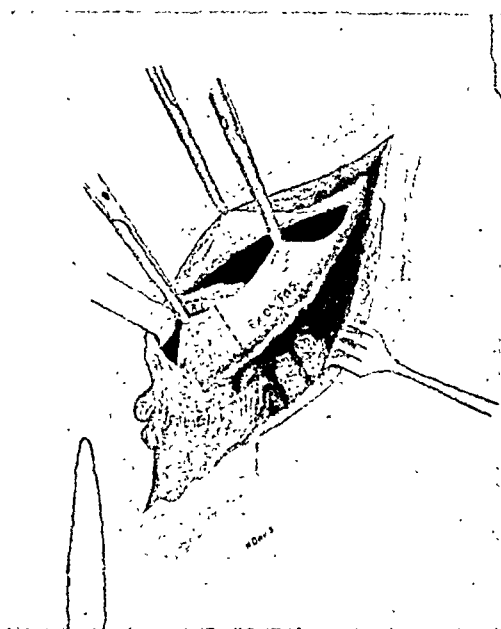


Fig. 20.—Basset's operation (step 3). Fascia drawn up and femoral lymphatics with surrounding fat dissected free from saphenous vein down to the femoral ring. The dotted line indicates where the cut is made through Poupart's ligament. *F. L. Gl.*, femoral lymph glands; *F.V.*, femoral vein; *F.A.*, femoral artery; *Ex. Ob. Fas.*, external oblique fascia.

removed in continuity with the round ligament which is ligated before being cut. Care should be taken at this point not to cut the important nerve trunks running parallel to the incision.

3. After clamps are placed on the fascia above the femoral ring, Poupart's ligament is drawn up and cut 1 cm. internal to the femoral vein. The two ends of the ligament are now drawn apart and the inferior epigastric vessels tied off closely to their origin from the iliac. The lymph gland of Cloquet, situated close to the femoral vein, is thus exposed and can readily be freed from its attachments. It is important, however, to retain its connection with the lymph channels running directly to the clitoris from this point. To do this will occasionally necessitate an additional skin incision downward to the region of Bartholin's gland. All the lymph glands in Scarpa's triangle should be dissected free. Thus the entire inguinal

and femoral lymph glands are laid bare in continuity with the tissues of the external genitals.

4. The closure of the inguinal wound can now be undertaken, first bringing the ends of Poupart's ligament together, and suturing them to the aponeurosis of the pectineus muscle, without, however, compressing the femoral vein. Now the transverse and oblique muscles of the abdominal wall are sutured to Poupart's ligament as in a hernia operation, and the aponeurosis of the external oblique muscle sutured over the top of the ligament.

The further steps of the operation consist of the removal of the primary growth of the vulva and need not be described in detail. A similar dissection of the lymph gland chain on the opposite side should precede the excision of the primary tumor.

*Anesthesia.*—The duration of the operation makes it desirable in these old women to get along with the minimum amount of general anesthesia. A good twilight to start with is of great advantage. A few

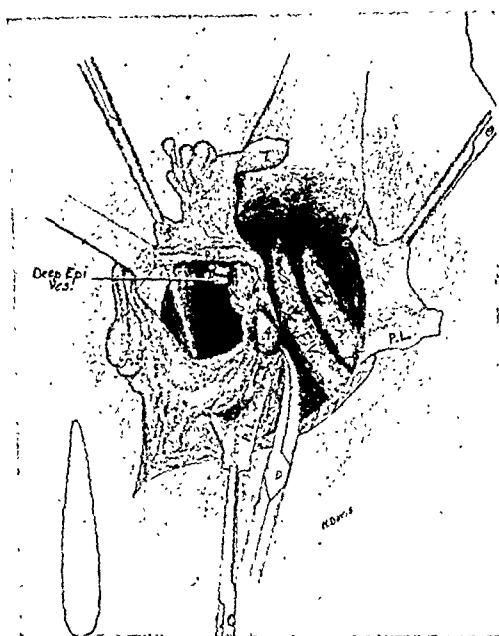


Fig. 21.—Basset's operation (step 4). Poupart's ligament with the lower flap of the external oblique fascia has been divided and drawn apart to expose Cloquet's gland just within the femoral ring. The inguinal lymphatics running along the round ligament have been dissected free. The deep epigastric vessels have been ligated and cut near their origin from the external iliac vessels. After resecting the round ligament and shelling out the gland of Cloquet, the whole mass is excised. The ends of Poupart's ligament are then sutured together and the oblique muscle fastened to it as in the operation for inguinal hernia. *P.L.*, Poupart's ligament; *F.A.*, femoral artery; *F.V.*, femoral vein; *R.L.*, round ligament; *Deep Epi. Ves.*, deep epigastric vessels; (1) deep inguinal gland (lateral to vessels); (2) inguinal glands along round ligament; (3) superficial femoral glands; (4) deep femoral gland or gland of Cloquet.

cases were done under spinal anesthesia. Local anesthesia can in most cases be used with good results and is I believe preferable, even if a small amount of general anesthesia has to be employed in addition.

*Postoperative Care.*—A retention catheter is usually inserted for the first forty-eight hours to avoid external manipulations during this time. If the perineoanal skin has been removed, it is well to put the patients on a diet that will keep the bowels from moving for a period of ten days. Of great importance is the question of dressings. Dry dressings

TABLE I. ANALYSIS OF FIVE-YEAR CASES OF VULVAL CANCER (1907-1923)

	TOTAL CASES	OPERATIVE DEATHS	DIED WITHIN 1 YEAR	DIED BETWEEN 1 AND 5 YEARS	DIED AFTER 5 YEARS	DIED OF OTHER CAUSES WITHIN 5 YEARS	CURED FOR 5 YEARS OR MORE	NOT TRACED	PERCENTAGE CURABILITY 5-YEAR AND ABSOLUTE
Palliative or refused treatment	4	-	1	1	-	-	0	2	0
X-ray or radium	15	-	11	2	-	-	0	2	0
Simple vulvectomy	6	1	3	-	-	-	-	2	0
Vulvectomy with superficial or incomplete gland removal	13	1	3	3	1	1 (4 yr. later)	4	1	30.7 (5-year) 23 (absolute)
Vulvectomy with complete double-sided Bassett operation	11	0	1	1	2		9	0	81.8 (5-year) 63.6 (absolute)
Total cases	49	2	19	7	3	1	13	7	26.5 (5-year) 20.4 (absolute)

are applied for the first twenty-four hours but after that time there is so much wound secretion that it stagnates upon the dressings predisposing to wound infection and necrosis. I have, therefore, in recent years removed the dressings on the morning following the operation and kept the wound uncovered, protecting it from contact with the bedclothing by means of a wire frame in which is placed a lamp sufficient to keep the air warm and dry. In the evening dry dressings are placed over the wound and kept on during the night, to be removed on the following morning. Twice a day the wound is thoroughly irrigated with boric acid solution. Half strength tincture of iodine or 10 per cent silver nitrate or mercurochrome can be applied from time to time as indications arise. It is practically impossible to get primary wound healing in these cases but the necrosis and infection are markedly reduced by this method of treatment. In spite of frequent wound infection, I have had only one small hernia after the Basset operations, so that it does not appear that the cutting of Poupart's ligament is to be feared.

*Five-Year Results.*—The value of any method of treatment of cancer is based largely on the number of five-year cures obtained. If 7 out of the 49 cases in this group treated from 1906 to 1924 were not traced, this was largely due to the absence of a social service department in the earlier years of our hospital. In recent years every case is very closely followed up, reporting for reexamination every two to three months. The fate of the remaining 42 women is outlined in Tables I and II. From this it will be seen that no cures were obtained in any of the 15 cases treated with radium or x-ray; they all died within one year. It should however be said in fairness that only a few of these women had an early lesion. Equally unsuccessful were the cases in which a simple vulvectomy was done. None of the 6 cases passed the five-year period. Another group of 13 cases were those in which a superficial, one-sided or incomplete gland removal accompanied the vulvectomy. In one of these cases a Basset operation was attempted but owing to the invasion of a cancerous gland into the femoral sheath, this could not be carried out, hence it was included as an incomplete gland removal. Out of these 13 cases, four were free of recurrence longer than five years (30 per cent), but one died the following year of some bowel trouble. Striking were the results obtained in the 11 patients upon whom a Basset was done in addition to the vulvectomy. Of this number 9 remained free of recurrence longer than five years (81 per cent). Two women however developed a late recurrence, one at five and one-half years, from which she died and the other one at eight years. The latter after apparently complete removal of a small, local recurrence (new cancer?) died of an influenza pneumonia shortly afterward. Even so, we have left seven women free of recurrence at the present time, an absolute curability of 63.6 per cent with this type of operation.

TABLE II. SUMMARY OF BASSET OPERATIONS

CASE	AGE CHIL- DREN	CLIN- ICAL GROUP	MALIG- NANCY INDEX	SYMPTOMS COURSE	INVOLVEMENT	OPERATION	CANCER GLANDS	SUBSEQUENT RECORD
R. K. 1 Barnard 15217	35 5-ch.	2	1	Leucovulvitis for 8 years. Ulcer 8 months	Entire right labia. Ulcer 10 x 6 cm.	Vulvectomy and glands 10/12/15	None	Clinically cured Feb. 14, 1928 (13 years)
D. 2 Barnard 17070	43 4-ch.	4	3	Trauma 1 year previous. Wass. 4+	Very large right side mass, many large glands	1/22/17 Basset. 2/5/17 Vulvec- tomy	Very many	Died recurrence Dec. 1917
G. 3 Barnard 22009	39 0-ch.	1	2	Pruritus 1 year. Sore recently	Small ulcer 1 to 2 cm. left labia. Leucovulvitis	Radium (1200 mg.) 8/14/20. Basset and vul- vectomy 9/23/20	None	Carcinoma at anal margin. Second operation 9/12/23. Clinically well. 1/30/29 (5 years)
M. 4 Barnard 22502	60 5-ch.	1	2	No pruritus. Pimple on vulva 1 year	Cauliflower 3 cm. in right labia. Leuco- kraurosis	Vulvectomy and Basset 11/24/20	None	Small new carcinoma near urethra 8/10/28 removed. Died pneumonia 12/8/28 (8 years)
S. 5 Barnard 23194	51 0-ch.	3	3	No pruritus. Lump on vulva 7 months	Rt. Bartholin gland tumor 4-5 cm. Glands large	Vulvectomy 4/30/21 Basset 7/20/21	Several	Recurrence (glands) 10/27/26 (5½ yr.) Died Dec., 1926
G. 6 Barnard 27083	71 0-ch.	2	1	Tumor on vulva 5 months	Ulcer 4 cm. left labia. Leucoplastic vulvitis	Vulvectomy and Basset 7/3/23	Present (left side)	Clinically well 3/12/29 (5½ years)
S. 7 Barnard 26664	73 12-ch.	2	2	Pruritus 2 years. Sore right side recently	Ulcer 5 cm. Prepuce and labia minora. Leucovulvitis	Vulvectomy and Basset 4/13/23	Tuberculosis. No carcinoma	Clinically well 3/1/29 (6 years)
P. 8 Barnard 27141	46 3-ch.	1	2	Burning urination. Bleeding 2 months	Ulcer 2 to 3 cm. Vestibule around meatus urin.	Vulvectomy. Resect urethra. Basset 7/11/23	None	Clinically well 1/25/29 (5½ years)

TABLE II.—CONT'D

CASE	AGE CHIL- DREN	CLIN- ICAL GROUP	MALIG- NANCY INDEX	SYMPTOMS COURSE	INVOLVEMENT	OPERATION	CANCER GLANDS	SUBSEQUENT RECORD
T. 9 Barnard 27968	63 0-ch.	1	2	Irritation near urethra 3 years	Ulcer 2 cm. Vestibule near meatus	Vulvectomy and Basset 11/14/23	None	Clinically well 2/28/29 (5 years)
E. 10 (private)	74 7-ch.	3	3	Pruritus 1 year. Lump 3 months	Ulcer 8 cm. infiltra- tion. Left labia. Leucovulvitis	Vulvectomy Basset 4/7/23. 4/21/23	Very many	Recurrence Feb., 1924. Died April, 1925 (1 year)
C. 11 (private)	65 0-ch.	1	2	Pruritus 20 years. Lump 1 year ago. Radium 10 months. Ex- cision 2 months	Recurrent. Ulcer 2 cm. right labia. Leucokraurosis	Vulvectomy Basset 1/31/24. Basset 2/16/24	Present left side	Keratosis removed 12/2/25. Clinically well April, 1929 (5 years)
S. 12 Barnard 32019	54 5-ch.	3	3	Pruritus and leuco- vulvitis	Tumor 7 x 7 cm. Left labia. Large inguinal glands	Vulvectomy Basset 9/4/25. 9/22/25	Very many	Recurrent. Died. 10/2/27 (2 years)
M. E. 13 Barnard 37534	55 0-ch.	3	1	Abscess left Barth. gland 13 yr. Lump 2 years	Tumor 8 x 6. Left Barth. gland in- volving rectum. Glands large	Vulvectomy and radium 12/16/27. Bas- set 12/21/27	Many	May 10, 1929 no re- currence (1½ years)
G. 14 Barnard 38123	Colored 43 1-ch.	1	2	Pruritus 4 years. X-ray for pruri- tus 5/14 to 6/29/28	Ulcer 1 cm. on leuco- plakia of prepuce and labia minora	Vulvectomy Basset 9/21/28. Basset 10/9/28	Present right side	No recurrence April, 1929 (6 months)
M. 15 Barnes Hospital	Colored 45 1-ch.	1	1	Nodule on vulva cut 4 years ago. Frequent cau- tery. Did not heal	Ulcer 1 to 2 cm. left labium minus	Diagnostic excision 4/11/29. Vul- vectomy and Basset 4/25/29	Examination not complete	Too recent
K. R. 16 Barnard 36400	43 5-ch.	2	1	Pruritus several years	Ulcer 4 cm. left labia leucokraurosis	Vulvectomy 7/12/27. Basset 5/14/29	Examination not complete	Too recent



Unfortunately we have few statistics from other clinics with which to compare these results. In Bonn from 1912 to 1921, Schmidt reports only two out of 13 cases free of recurrence. Giesecke from the Kiel clinic reported 25 cases operated upon longer than five years ago, 10 of whom remained free of recurrence (40 per cent). Giesecke in 15 of these 25 cases employed the radical Stoeckel type of operation.

A more detailed statement concerning those patients operated upon by the Basset technic, given in Table II, will bring out other interesting points. The first 11 of the 16 cases were all operated upon more than five years ago. It will be noted that only 5 out of the 11 were in Group I, the very early cases, 3 were in Group II, 2 were in Group III and one was so far advanced that it was included in Group IV. From this it is evident that these cases have not been selected ones. It is further to be noted that every one of the 8 cases in Groups I and II remained free of recurrence for over five years, the only recurrence in this group was the one that occurred eight years after operation and is probably to be more rightly considered a new cancer. The malignancy index in these cases corresponds fairly closely to the clinical group.

The most convincing evidence of the value of the Basset operation is that in two of the cases that are still clinically cured, over five years ago there was found on microscopic examination carcinoma in the removed lymph glands. In Figs. 17-A and B is seen a microphotograph of one of these gland metastases.

#### SUMMARY AND CONCLUSIONS

Leucoplakic vulvitis appears usually in women shortly after the menopause. It may involve the entire vulva or appear in symmetrical or irregular patches. In over one-half of the cases there is an obliteration of the labial and preputial folds known as kraurosis. Pruritus of long standing is the most pronounced symptom. The disease is very rare in the negro race. In over one-half of the cases it leads to the development of carcinoma.

Further clinical and histologic studies tend to confirm the views previously expressed that the underlying cause of leucoplakic vulvitis is a loss of elasticity in the skin due in part to deficiency of ovarian hormones. This defect in the elastic structure leads to increased friability with resulting cracks and abrasions. Through these openings bacteria gain entrance and pruritus results. The scratching then increases the infection by providing new ports of entry. The chronic vulvitis thus produced leads to hyperplasias (keratosis, acanthosis) and later to atrophies (sclerosis, collagen formation, kraurosis).

The treatment of leucoplakic vulvitis, both on its own account and as a precancerous lesion, consists of excision of the affected vulval skin. The five-year results after such a vulvectomy are uniformly favorable and justify the discomforts attendant upon the operation.

These discomforts have been greatly reduced by two modifications in technic, the use of a vaginal flap over the perineum and the retention of a double anal bridge in cases of perianal involvement.

Cancer of the vulva is not a pathologic entity. There are 4 well defined types: (1) *epidermal*, springing from the labial, preputial or perineal skin, associated almost always with leucoplakic vulvitis; (2) *clitoris*, springing from that organ itself (not from the prepuce) a very rare and malignant form; (3) *vestibular*, arising from the vaginal introitus, usually springing from old syphilitic ulcers in relatively young persons; (4) *Bartholin gland*, also rare, usually after chronic Bartholinitis.

A division of the 76 cases in my series according to clinical involvement, showed that about 60 per cent were operable. A division of the cases according to the histologic malignancy index showed that this corresponded closely with the extent of the clinical involvement. It also showed that the cancers on a leucoplakic basis were relatively benign, whereas those springing from syphilitic ulcers, were very malignant.

The treatment of cancer of the vulva by radiotherapy has been very unsuccessful. Burns readily occur and retrogressions are few and temporary. Surgery is alone to be considered unless the patient's condition makes this impossible. Simple vulvectomies or superficial or one-sided gland dissections meet with a high percentage of recurrences. The double-sided Basset technic of gland removal together with vulvectomy is a safe operation followed by a high percentage of five-year cures (81.8 per cent in my series). Two cases with gland metastasis are among these cures. The vulvectomy must be complete in every leucoplakic case, since a new cancer may arise years later from a remaining island of leucoplakic skin.

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# A CLINICAL AND ANATOMIC DESCRIPTION OF A NAEGELE PELVIS

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THE rarity of this type of pelvis, the beauty of our specimen, as well as certain interesting points in the clinical history of the patient from whom it was obtained, seem to justify its description.

*Clinical Data.*—The patient, B. T., Unit No. 17,583, had been under observation from 1917 to the time of her death in April, 1928. When first seen she was sixteen years of age, presented no striking external deformity, nor did anything in her previous history suggest the possibility of any unusual complication.

On her first admission, pelvic mensuration apparently showed a generally contracted funnel pelvis, with a distance of 7.25 cm. between the tubera ischii, with the head engaged in L.O.P. On March 17, 1917, she had a spontaneous labor lasting twenty-one hours, the occiput rotating into the hollow of the sacrum. The child weighed 2600 grams, presented a biparietal diameter of 8.25 cm., and at the end of the puerperium was discharged with its mother in good condition.

In December, 1918, a second spontaneous labor occurred. After a second stage of one hour and forty minutes, the child was expelled in L.O.A., when it was noted that only the lower portion of the pubic arch was occupied by the occiput. Again, the child was small, weighing 2890 grams and having a biparietal diameter of 8.75 cm.

On a ward visit shortly before her discharge, I saw the patient walking about and noted that her body had a "list" to the left. Upon inquiry, I was informed that she had a generally contracted pelvis and was convalescing from a second uneventful labor. As my curiosity was aroused, I examined her carefully, and eventually made the diagnosis of a Naeglele pelvis, and dictated the following note: "On inspection there is a slight scoliosis in the lumbar region with its convexity to the left. There is slight asymmetry in the pelvic region, the left buttock appearing less well developed than the right. There is slight tilting of the pelvis, as the distance from the iliac crest to the floor measures 102 cm. on the right, and 101 cm. on the left side. The distance from the right anterior superior spine to the left posterior superior spine is 2 cm. greater than the corresponding measurement on the opposite side. Likewise, the distance from the spine of the last lumbar vertebra is 2.25 cm. greater to the right than to the left anterior superior spine, while there is a similar difference in the measurements between the tip of the sacrum and each of the ischial tuberosities.

"With the patient in lithotomy position, there is slight asymmetry of the pubic arch, as the left ischiopubic ramus extends outward at a sharper angle than the right. The symphysis pubis is vertical. On internal examination, the sacrum is felt throughout its entire extent, the promontory is readily palpable, and the diagonal conjugate measures 11.5 cm. The entire linea terminalis can be palpated. On the left it extends obliquely backward in a straight line and terminates about 1 cm. to the left of the body of the first sacral vertebra. On the right side the terminal line presents the usual concavity and terminates posteriorly 2.5 cm. to the right of the body of the first sacral vertebra. It is impossible to ascertain the condition of the sacroiliac joints, but there is clearly a radical difference between the two sides. Both ischial spines are readily felt, and the left one approaches the sacral

margin closer than the right. In general, it may be said that the pelvis is Naegele in character, and that the superior strait roughly corresponds to the accompanying sketch. (Not reproduced.) While the symphysis pubis does not appear asymmetrical, the conjugata vera extends obliquely to the left, the sacral promontory lying several centimeters to the left of a line extending sagittally backward from the top of the symphysis."

Fig. 1 shows the front and back views of the patient, while Fig. 2 is a reproduction of the x-ray print which was taken at that time, and which confirmed the diagnosis.

Following this, the patient was not seen again until 1926, although she stated that during the intervening period (1920, 1921, and 1923) she had had three

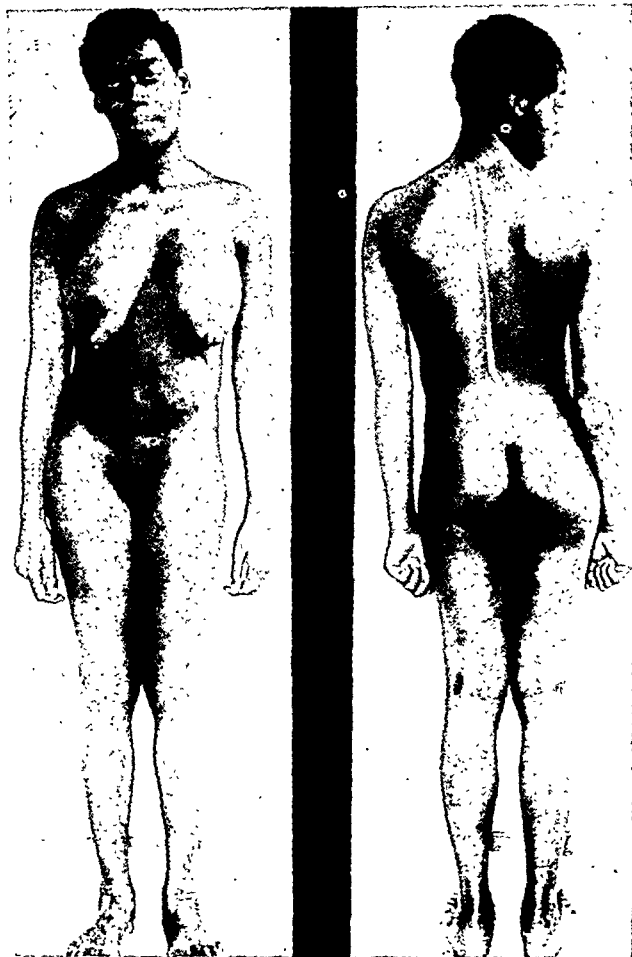


Fig. 1.—Front and rear views of patient. Note tilt to left of torso.

spontaneous labors at home under the care of a midwife, and that all of the children were small. On April 18, 1926, her sixth pregnancy terminated spontaneously at home under the care of our Out-Patient Service. At that time the child presented in R.O.A. and was born uneventfully after a labor of eight hours. Again, it was small, weighing 2900 grams, with a biparietal diameter of 8 cm.

The patient was next seen in January, 1928, when she applied to the Prenatal Clinic for care in her approaching seventh delivery. The assistant in charge, being led astray by the history of repeated spontaneous labors, failed to look up the previous histories and thus overlooked the existence of the Naegele pelvis. A

diagnosis of a moderately generally contracted funnel pelvis having been made, it was arranged that the patient should be delivered in her own home by the Out-Patient Service. She fell into labor on March 17, 1928, with the child in R.O.A. Seventeen hours later the cervix was found to be fully dilated, with the head at the level of the spines. As no advance had occurred at the end of two more hours, the assistant decided to apply forceps. As he experienced difficulty in doing so, he gave up the attempt, and extracted a live child after what he termed an easy version. The placenta did not separate spontaneously, and, as several attempts at Credé expression were ineffectual, manual removal was resorted to one hour after delivery. The patient was watched for a further hour, and was left in apparently excellent condition. The child was large, weighing 3400 grams and having a biparietal diameter of 9.5 cm.

Some hours later, word was sent to the Clinic that the patient was not doing well, and, when seen by the externe, she was found to be so seriously ill, with rapid pulse and painful and distended abdomen, that she was at once brought to the clinic. I saw her shortly after admission, made a diagnosis of traumatic rupture of the

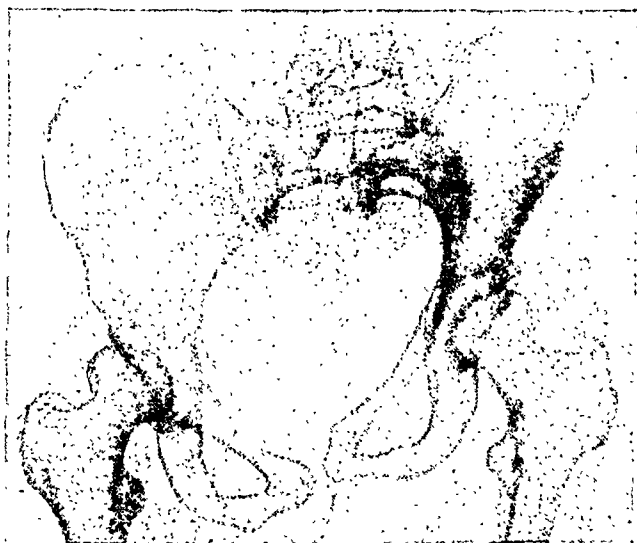


Fig. 2.—Reconstruction of x-ray of patient.

uterus with intraabdominal bleeding, and operated as soon as the necessary preparations could be made. On opening the abdomen large quantities of free blood were present, and the uterus was found to be ruptured through the right and anterior portion of the lower segment. Supravaginal hysterectomy was done and the patient left the table in good condition. On the second day bronchopneumonia was diagnosed, and the temperature remained elevated until death occurred on the twenty-fifth day. At autopsy it was found that the patient had a tuberculous pneumonia, while a minor infective process had developed in the pelvic cavity. The entire pelvis was then removed, together with the last two lumbar vertebrae, and the upper ends of the femora.

To summarize, we had to deal with a patient having a typical Naegele pelvis, through which she had six spontaneous labors with small children, and who died after the operative delivery of a seventh child. In the first three of the four labors, which we conducted, the largest child weighed 2900 grams and had a biparietal diameter of 8.75 cm., while in

the last labor the child was much larger and weighed 3400 grams with a biparietal diameter of 9.5 cm. Upon studying the outlines and dimension of the pelvis, as shown in Figs. 3 to 5, it is apparent how spontaneous labor had occurred with the small children, and how it became impossible when the last child had attained more than average proportions.

Furthermore, our records show that the child presented in L.O.P., L.O.A., and R.O.A., in the first, second, and sixth labors respectively. Consideration of Fig. 3 shows that engagement could have occurred with the head in L.O.P. or R.O.A., as in either presentation its long diameter would occupy the left oblique diameter of the superior strait, which measures 11 cm., while the small biparietal diameter would accommodate itself, after some moulding, to the right oblique diameter of 8.4 cm. On the other hand, it does not appear probable that a child presenting in L.O.A. could undergo engagement. Consequently, as the history states that in the second labor the occiput was delivered anteriorly, it must be assumed that when labor set in, the occiput, which had originally rested upon the anterior portion of the slanting left linea terminalis, had slipped forward and eventually became engaged in R.O.A.

The tragic end of the last labor must be attributed to the carelessness of the assistant concerned, and demonstrates how difficult it is to conduct an ideal service. Had he taken the trouble to go over the previous histories, he would have found that he had to deal with an unusual pelvis, and automatically would have sent the patient into the clinic, where the disproportion would have been recognized and properly treated. Excuse for him may be found in the fact that the patient had already gone through six spontaneous labors, three being in the hands of a midwife; so that, in the absence of gross and striking abnormality, the presumption would be in favor of a similar outcome at the seventh delivery.

Finally, before passing on to a description of the pelvis, it should be mentioned that the patient walked without a limp. It is true that careful inspection did reveal an abnormal bodily habitus, but it was so slight as to escape detection by any but an acute observer. Furthermore, and especially in connection with the etiology of the deformity, stress should be laid upon the fact that there was nothing in the history to indicate that the patient had at any time suffered from inflammatory bone disease. After her death her husband and elder sister were carefully questioned on this point, and both stated that she had at no time been bedridden, nor had she ever complained of any disturbance in locomotion; on the contrary, they claimed that she was "light upon her feet" and quick in all her movements. Finally, careful inspection of Fig. 1 fails to reveal any trace of scars about the thighs,

buttocks or groins, which might have directed attention to a preexisting inflammatory process about the sacroiliac joint.

*Description of Pelvis.*—Figs. 3, 4 and 5 make it clear that we have to deal with a typical Naegele or obliquely ovate pelvis, in which the left sacroiliac joint has been obliterated, a considerable part of the left ala of the sacrum has disappeared, and what remains of it has become firmly synostosed with the left innominate bone.

The extent of the obliquity is shown by the following measurements:

Left anterior superior to right posterior superior spine 15.75 cm.

Right anterior superior to left posterior superior spine 19.75 cm.

Tip of spinous process of first sacral vertebra to left anterior superior spine 13.5 cm.

Tip of spinous process of first sacral vertebra to right anterior superior spine 16.0 cm.

Center of promontory to right sacroiliac joint 5 cm.

Center of promontory to left sacroiliac joint 3 cm.

Center of promontory to right iliopectineal eminence 9.3 cm.



Fig. 3.—Naegele pelvis, superior strait  $\times \frac{1}{2}$ .

Center of promontory to left iliopectineal eminence 6.0 cm.

Tip of sacrum to right ischial spine 8.1 cm.

Tip of sacrum to left ischial spine 5.7 cm.

The entire pelvis is somewhat smaller than usual, as is shown by the following measurements: Distance between anterior superior spines 18 cm.; between iliac crests 20.5 cm., and Baudeloeque diameter 18.75 cm. At first glance, it might appear that the left innominate bone is somewhat atrophic as compared with the right, but mensuration shows that such is not the case, as the two sides present practically identical measurements which in no place differ by more than one-half centimeter. Thus, the length of the iliac crests, as measured between the anterior and posterior spines by a pelvimeter, is 14 cm. on the right and 13.5 cm. on the left side. Likewise, the distance between the ends of the pubic bone and the corresponding anterior superior spine of the ilium is 17.2 cm. on the right, and 17.5 cm. on the left side. Finally, the height of the pelvis, as measured from the center of the tuber ischii to the highest point of the corresponding iliac crest, is 18.5 cm. on the right and 18.75 cm. on the left side.

Fig. 3, which represents the superior strait, shows the characteristic obliquely ovate form, and illustrates a number of features which are familiar to those acquainted with the Naegele pelvis. In the first place the ileopectineal line on the right side presents an exaggeration of the normal curvature, as contrasted with its almost straight course on the abnormal side. As a consequence, the symphysis pubis lies eccentrically, so that the anterior termination of the conjugata vera is formed by the tip of the right pubic bone. It will also be noticed that while the terminal length is practically identical on the two sides (right 18.4 and left 18.6 cm.), the dimensions of its component parts differ considerably. Thus, on the right side the pubic, iliac, and sacral portions measure 6.5, 5.8, and 6 cm. respectively, as compared with 6.5, 5.1 and 7 cm. on the abnormal side. In other words, while the pubic portions are identical on both sides, the iliac portion is 7 mm. shorter and the sacral portion 10 mm. longer on the abnormal side. This is in accordance with the observations of Breus and Kolisko, who claim that it is the general rule, and is due to the fact that, owing to the absence of the articular facies of the ilium, the growth of the iliac portion of the terminal length is defective, with the result



Fig. 4.—Naegele pelvis, front view  $\times \frac{1}{4}$ .

that the ala of the sacrum does not become displaced backward during the growth of the pelvis, so that the sacral portion of the terminal length remains longer than usual. This observation is also confirmed by reference to Fig. 5, which shows that the posterior extremity of the iliac crest projects 7 millimeters further beyond the posterior surface of the sacrum on the abnormal than on the normal side.

Fig. 3 shows the distortion of the superior strait, whose usual diameters present the following measurements: conjugata vera 11.4 cm., transverse 9.5 cm., right oblique 8.4 cm., and left oblique 11 cm. It will be noticed that the conjugata vera extends obliquely backward from the inner surface of the tip of the right pubic bone to the center of the promontory of the sacrum, whereas a line drawn directly backward from its anterior termination practically bisects the right sacral ala.

Fig. 4 shows that the sacrum measures 10 centimeters from promontory to tip, and that its long axis is oblique instead of vertical, with its upper end approaching the left, and its lower end the right side of the pelvis. The most impressive feature of this aspect of the pelvis, however, consists in the radical changes which have taken



place in the region of the left sacroiliac joint, which has become entirely obliterated, while the left sacral ala is only a fraction as broad as the right, the destruction being much more pronounced in its anterior portion.

It will further be noticed that where fusion has occurred, the surface of the bone presents a burnished appearance, almost as if it had been artificially polished, and gives no suggestion that the ankylosis had followed an inflammatory process. Furthermore, it will be noticed that on the normal side the bodies of three sacral vertebrae take part in the formation of the joint, whereas on the fused side only two are involved.

In connection with the sacroiliac joints, consideration of Figs. 3 and 4 will show that on the normal side the upper margin of the articular facies of the ilium is in contact with a similar articular surface of the sacrum for a distance of 3 centimeters, while beyond it there is a free portion which extends backward for a distance of 17 millimeters. On the abnormal side there is no joint surface, but the sacrum



Fig. 5.—Naegele pelvis, inferior strait  $\times \frac{1}{4}$ .

and ilium have become intimately fused for a distance of 4.7 cm. It may also be noticed at the extreme posterior end of the line of fusion that there is a roughened elevation of porous bone (10 by 6 by 3 mm.), which to my mind constitutes the only evidence that can be adduced in support of the supposition that an ostitic process had ever existed in this locality.

On casual inspection of Fig. 4, it might appear that the pubic arch is asymmetrical, with the left ischiopubic ramus shorter than the right. Mensuration, however, shows that such is not the case, as there is a difference of only 2 millimeters in the length of the two rami. There also appears to be a marked difference between the two acetabula, and it is evident that the left one is directed more anteriorly than the right. On the other hand, the apparently greater depth of the posterior aspect of the articular surface of the left acetabulum has no existence in fact, as mensuration shows that it is actually shallower than on the right side (2.4 to 2.7 cm.).

Fig. 5 gives a good idea of the distortion of the inferior strait, except that it seems to show that the distance between the ischial spines is shorter than between

the tubera ischii; whereas in reality the former measures 8.3 as compared with 8 cm. Attention has already been directed to the greater extent to which the posterior end of the left iliac crest projects beyond the posterior surface of the sacrum, as well as to the views of Breus and Kolisko concerning its incidence and significance.

As was previously stated, the last two lumbar vertebrae were removed with the specimen, and when they are placed in position it appears that a slight scoliosis must have existed during life, with its convexity low down on the left side. As will be pointed out in the next section, the scoliosis is less pronounced than would have been expected. That a pronounced disturbance in the statics of the pelvis had existed during life is shown by the status of the two superior articular facets of the first sacral vertebrae. Fig. 3 shows that their attitude is not altered, as indicated by their inclination to the midline, but inspection reveals that they differ materially both in shape and size. Thus, the right articular facet is oval in shape, with its long diameter extending transversely, and measures 20 by 13 millimeters; while the left facet is roughly quadrilateral in outline, with its long diameter vertical, and measures only 15 by 13 millimeters. From this it would appear that better mechanical conditions had existed on the right than on the left side, which may have had an important bearing upon the unimpaired locomotion of the patient.

*Implications.*—In Naegele's original monograph, which appeared ninety years ago, the description of the morphology of the obliquely ovate pelvis was so masterly that nothing has since been added to it. As is well known, Naegele attributed the deformity to a congenital defect involving one ala of the sacrum with resulting imperfect development of the sacral portion of the sacroiliac joint. Furthermore, when the individual began to move about, the body weight would in great part be transmitted to the femur on the affected side, with the result that unusual pressure would be exerted upon the abnormal joint, and that the irritation induced thereby would eventually lead to ankylosis. His original publication was followed by a considerable literature, and all of the earlier contributions were confirmatory of his point of view. Indeed, it was not until 1861 that any scepticism developed, when Thomas of Leyden pointed out that in at least a certain proportion of obliquely ovate pelves the essential feature lay in the destruction and subsequent fusion of an originally normal sacrum as the result of inflammatory disease, rather than in a primary defect in development.

Since then the discussion has continued, and reached its culmination in 1900, when Breus and Kolisko in their monumental work on deformed pelves stated that the condition is always the result of inflammatory disease, whose existence can generally be elicited from the history of the patient, and particularly from the presence upon the external surface of her body of cicatrices which indubitably indicate that such disease had existed.

In the second volume of their great work, 203 pages are devoted to the consideration of "Ostitic and Synostitic Pelves," and 147 of them are concerned entirely with the Naegele pelvis. In the first part of their study it is clearly shown that all sorts of deformity may follow

tuberculous or other inflammatory destruction about the sacroiliac joint, which when extreme may eventuate in the production of the characteristic Naegele deformity. In many specimens the inflammatory nature of the condition is demonstrated by the presence of irregularly shaped deposits of callus, which admit of no other interpretation, and frequently is still further confirmed by the presence of cicatrices which mark the location of old sinus tracts. Indeed, Breus and Kolisko go so far as to believe that all examples of the so-called Naegele pelvis are ostitic in origin and state that in their extensive studies they could find no evidence that the congenital defect described by Naegele is ever concerned in its production. Furthermore, they hold in the rare instances in which such developmental defects do occur that they uniformly give rise to pelves of totally different character.

After carefully studying the pelvis here described, it occurred to me that it might be of interest to attempt to ascertain in how far it serves to support the contentions of Breus and Kolisko. At this point, I think it only fair to admit that my studies have led to no definitive conclusions, and that the most that can be claimed from them is that they tend to indicate in a certain proportion of cases, at least, that a final conclusion is not so easily reached as one might gather from their sweeping conclusions.

In the first place, inspection of this specimen does not show any evident signs of the existence of a previous inflammatory process, and the only thing which could possibly be suggested in support of such a view is the presence of a small irregularly rounded elevation made up of porous bone at the upper and posterior margin of the ankylosed area. This, however, cannot be regarded as convincing, since areas of similar consistency are frequently noted in otherwise normal pelves.

The second point opposed to the inflammatory etiology of the deformity is afforded by the history and inspection of the patient. As has already been indicated she walked without a limp, and after her death her husband stated that she had never mentioned that she had suffered from any form of bone disease during childhood. Furthermore, her older sister confirmed these statements, and stated that the patient had learned to walk at the usual age, had never limped, nor complained of any trouble in locomotion, but, on the contrary, had always been very light on her feet. Such a history is of considerable importance, as it is scarcely conceivable that an inflammatory lesion, sufficiently severe to bring about the extensive destruction of tissue necessary to produce the deformity, could have existed without giving rise to clinical symptoms or without necessitating a prolonged stay in bed.

With this point in mind, the exterior of the body was carefully examined at the time of autopsy with a view to detecting any cicatrices, which might have followed an ostitic process, but none were found. Furthermore, inspection of Fig. 1, which reproduces the photograph taken after the second labor, shows that none were discoverable in 1918.

Still more conclusive negative evidence is afforded by Fig. 6, which represents an x-ray picture of the upper portion of the region involved, which was kindly taken by Dr. Eben C. Hill, Lecturer in Roentgenological Anatomy. This type of investigation was adopted in the hope that the bony architecture might make it possible to draw some conclusion as to what had previously taken place in that locality. The figure clearly shows that the bony fibers extend continuously from the sacrum into the adjacent ilium, and pursue so regular a course that Dr. Hill does not consider their arrangement compatible with a previous inflammatory process, as he holds that had the ankylosis occurred subsequent to it the course of the fibers must have exhibited some interruption

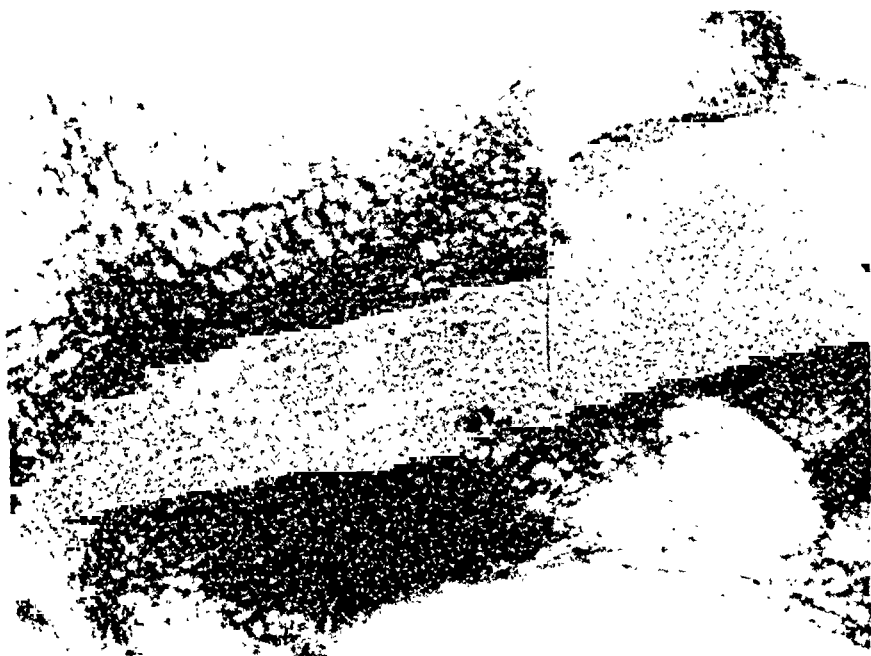


Fig. 6.—X-ray showing bony architecture of left sacroiliac region.

or irregularity. Possibly additional information might have been elicited had sections been made through the region involved, but the specimen was so valuable that I hesitated to sacrifice it for scientific purposes.

Summing up our findings in this regard, it seems safe to say from the history of the patient, the absence of cicatrices, the gross appearance of the specimen, as well as from the x-ray findings, that it seems impossible that the patient had suffered from a serious inflammatory bone lesion after birth, and consequently it seems likely that the deformity must be attributed to conditions which came into play during antenatal life—in other words, that it is congenital. On the other hand, our knowledge is unfortunately too defective to permit even a guess as to its nature, so that I shall content myself by stating that the contentions of

Breus and Kolisko do not seem to apply to our specimen, and that it is probable that their generalizations must share the fate of all exclusive statements—namely, that while they are usually correct, they do not necessarily apply to the individual case.

Attention has already been directed to the fact that the bearer of this pelvis, in common with others mentioned in the literature, did not limp, and the question arises as to how so striking a deformity is compatible with a normal gait. Breus and Kolisko have devoted considerable attention to the problem, and believe that its solution is to be found in the fact that the scoliosis which develops in the lumbar region is compensated for by a second curve higher up in the vertebral column, with its convexity in the opposite direction, with the result that the symphysis pubis occupies the midline of the body, while the body weight instead of being transmitted directly to the promontory of the sacrum comes to be transmitted along a vertical line extending somewhere between the promontory and the normal sacroiliac joint. In this way, the body weight will be transmitted with almost equal force to the heads of the two femora, and consequently, the patient will limp but slightly, if at all.

Do such considerations apply to this pelvis? Reverting to Fig. 1, it is seen that the vulva, and inferentially the symphysis pubis, occupies the midline of the body, but that the entire torso is somewhat tilted toward the left. On inspecting the dorsal aspect of the patient, it is seen that the lumbar scoliosis is scarcely apparent, and that the vertebral column above it, instead of presenting a compensatory scoliosis as postulated by Breus and Kolisko, continues to diverge toward the left up to the last cervical vertebra, which according to their contention should have led to an unequal distribution of the body weight, and consequently to a limp. Yet it has been repeatedly stated that our patient did not limp.

The only explanation which I can offer for this apparent contradiction of terms is possibly afforded by the development of a compensatory process in the cervical portion of the vertebral column. Inspection of the frontal aspect of the patient, as depicted in Fig. 1, shows that the head and neck are so deflected toward the right side that a straight line drawn through the heels and the symphysis pubis and extending through the head, passes through the center of the left eye instead of through the center of the forehead. Whether such a habitus would suffice to restore the statics of the body to essentially normal conditions, I am unable to state. If it did, it would be contrary to the conditions laid down by Breus and Kolisko, and would afford another demonstration that their conclusions are not infallible.

## IMPORTANT PROCEDURES IN THE CONSERVATIVE TREATMENT OF ECLAMPSIA

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THE good results given by the widely separated methods of the conservative treatment of eclampsia, that is, the use of elimination by Tweedy and the use of sedatives by Stroganoff, indicate that the maternal organism will recover if the disease has not lasted too long and the damage has not been too great. The favorable and unfavorable reports of various clinics based on one or the other methods suggest that each case must be individualized and that both experience and judgment are necessary. Furthermore, obstetricians have recognized as a result of the high maternal mortality that mild cases if treated radically will show an increase in the mortality rate, and severe cases treated conservatively will continue to show a definite mortality if early death of the fetus does not take place or delivery occur. As a result, many have taken the good points of each treatment and by combining them and determining the type of case are beginning to get still more favorable results. They have also realized that certain severe cases must be handled by early delivery. The difficulty still persists, however, in that it is usually impossible to decide as to the severity of the case before too much damage may have occurred.

In our studies of the toxemias of pregnancy we have found that there are a mass of results reported, but that there is no uniformity. Therefore, from the beginning we have been collecting as much data on each case as time permitted and have constantly increased the variety of examination as our accumulated material gave fresh ideas or required additional confirmation. Our results indicate the need for certain specific treatment the use of which enables us to give a prognosis early enough to be of value. Much of this data is not included in this paper but will furnish the basis of an additional report.

Our treatment can be summarized as follows:

1.  $MgSO_4$  in 25 per cent solution is given intramuscularly to control convulsions. On admission we inject 10 c.c. and give 5 c.c. after each convulsion until controlled. Our average amount over a period of five years has been 19 c.c. with a maximum of 50 c.c. in only one case. In coma no  $MgSO_4$  is used, for we believe that its only action, if given intramuscularly, is as a sedative. If given intravenously it does decrease intracranial pressure, but its depressant action on the respiration and the heart are so marked that they contraindicate its use. Dorsett has given intramuscularly from 15 c.c. to 200 c.c. depending on the severity of the case. In three cases he gave 200 c.c. per twenty-four hours. We attribute our success with the

small dose in not only controlling the convulsion but also preventing their further occurrence to the use of intravenous glucose.

2. Believing that absorption from the alimentary tract is an important factor, we give a colonic irrigation and in addition usually wash out the stomach and leave 60 c.c. of a saturated solution of  $MgSO_4$  in it.

3. Our next, and most important procedure is to inject 1000 c.c. of a 20 per cent glucose solution intravenously over a period of thirty to fifty minutes, two, three, or even four times daily, depending on the severity of the case.

4. Usually after twenty-four hours, the stomach will empty itself as evidenced by failure to recover injected solution, and then we inject 5 per cent Karo syrup water beginning with 50 c.c. and increasing hourly up to the patient's tolerance which may be as much as 300 c.c. per hour. This is continued until the patient is conscious and able to take our eclamptic diet, which consists of fruit and fruit juices.

In Table I, we list data from a number of cases of eclampsia giving the findings (1) on admission, (2) at the time of greatest blood dilution, and (3) at discharge (which is at least three weeks postpartum). All of our cases on admission had a blood concentration as evidenced by high hemoglobin, cell volume percentage, and serum protein percentage. Case 2734 admitted and treated as a preeclamptic had blood findings which were normal for her period of gestation but during labor she had convulsions and blood taken at this time was concentrated.

Shortly after delivery, it has been demonstrated by numerous investigators, Zangemeister, Eckelt, Dienst, Stander and Tyler, Plass and Bogert, Thompson, and de Wesselow that a blood dilution occurs in which the cell volume, hemoglobin, protein, specific gravity, and certain of the inorganic constituents all take part. Our work indicates that this dilution occurs within twenty-four hours postpartum or after death of the fetus. It is during this period of blood dilution, with its accompanying physicochemical changes, that the greatest clinical improvement, greatest diuresis, and greatest weight loss take place. We find that the cell volume percentage drops 15 to 25 per cent while the protein decreases 25 to 35 per cent. Furthermore, the serum proteins return to normal within two weeks but the cell volume percentage and hemoglobin at the time of discharge, which is at least three weeks, have not returned to normal.

In the normal individual the urine represents approximately 90 to 100 per cent of the fluid ingested (Atwater); but in normal pregnancy it represents only 50 to 60 per cent (Slemons). Thus with such a high positive water balance required for the growing fetus, it is evident that any disturbance may have serious results, which may be edema or dehydration, depending on whether the balance is positive or negative. After delivery a diuresis occurs in which the urine represents 60 to 80 per cent of the water intake. Slemons reports that in a case in which the fetus was dead, the urine represented 93 per cent of the fluid intake. In the toxemic patient after delivery, the urine represents 90

to 100 per cent, and if the patient is edematous, it actually exceeds the intake. It is therefore evident that the diuresis is a physiologic phenomenon occurring only after delivery or death of the fetus and since its appearance is so intimately associated with clinical improvement, we consider its production of primary importance. Tables II and III are representative of typical changes in the blood and urine in eclampsia, especially after delivery; and Table IV of changes both before and after. In a number of cases we have succeeded in lowering the serum

TABLE I

NUMBER		DATE	HEMOGLOBIN	CELL VOLUME PER CENT	SERUM PROTEIN PER CENT	WEIGHT KILO.
F. F. 11738	1*	7/18/27	113	46.4	6	77.7
	2	7/19/27	102	34	3.82	
	3	8/17/27	81	40	6.35	62.3
E. D. 174	1	9/ 6/27	86	39	5.92	
	2	9/ 6/27	98	41	5.56	
	3	9/20/27	76	35	5.8	
E. B. 440	1	10/16/27	91	43	5.03	70.2
	2	10/21/27	65	30.8	4.42	
	3	10/25/27	74	32	5.12	
L. B. 715	1	11/24/27	83	40	6.81	
	2	11/29/27	66	35	6	
	3	12/ 7/27	70	36	5.85	
N. C. 1332	1	2/16/28	101	42	8.42	79
	2	2/17/28	72	28.8	4.93	
	3	2/29/28	82	30	7.5	67
M. W. 1760	1	4/10/28	111	42	6.4	166
	2	4/12/28	58	27	4.43	
	3	5/ 3/28	83	36	7.23	116
T. H. 1992	1	5/15/28	91	37	6.54	
	2	5/15/28	70	28	5.17	
	3	5/24/28	59	26	6.4	
McC. 2062	1	5/24/28	100	44	6.42	
	3	6/ 1/28	75	35	6.45	
W. P. 2734	1	8/12/28	63	34	5.13	71.2
	a	8/18/28	105	55	5.6	
	2	8/20/28	66	32	4.28	
	3	9/ 1/28	85	34	6.45	60
E. A. 3380	1	10/18/28	85	45	5.55	75
	b	10/19/28	119	49	5.52	
	2	10/20/28	105	41	4.15	
	3	11/ 5/28	98	35	6.26	
W. W. 3437	1	10/25/28		49	5.83	65
	2	10/30/28		32	4.8	58
	3	11/ 5/28		50	6.88	56.8
F. S. 3779	1	12/ 6/28	117	42	6.43	69.6
	2	12/ 8/28	90	36	5.45	
	3	12/10/28	111	38	6.73	
L. W. 4129	1	1/16/29	121	42	5.86	72
	2	1/21/29	83	31	4.84	
	3	2/ 8/29	100	40	6.36	49.5
M. B. 4640	1	4/ 2/29	105	40	7.47	69
	2	4/ 6/29	77	24	5.64	62
	3	4/22/29	64	27	6.92	

\*1. Admission; 2. Greatest Dilution; 3. Discharge; a. Convulsion; b. Aftertreatment.



protein concentration before delivery but we have never succeeded in producing the typical diuresis of 4000 c.c. or more except after delivery or death of the fetus. Table V demonstrates that identical changes can occur before delivery. In this case no fetal movements, were noticed by the mother after July 20, and it is a fair assumption that the fetus died on that day. This is supported by the fact that the urine increased steadily from 400 c.c. on the twentieth, to 2400 c.c. on the twenty-first, and reached a maximum of 6600 c.c. on the twenty-third, and then slowly dropped. No diuresis occurred after delivery on the twenty-seventh.

Our treatment differs from that described by other clinics in that we use large amounts of hypertonic glucose solution and it is to this that we ascribe not only our favorable results but also our ability to control the convulsion with small amounts of  $\text{MgSO}_4$ . Hypertonic glucose solution injected intravenously reduces intracranial pressure, which is usually markedly increased in eclampsia. (Zangemeister, Thies.) Hypertonic salt solution was first used by neurologic surgeons to lower the intracranial pressure but was discarded in favor of glucose because the latter is just as efficient, has no terminal increase in intracranial pressure as NaCl or Ringers has (Peet, Weed and McKibben, and Sachs and Belcher), and can be repeated more frequently because its end-products are  $\text{CO}_2$  and water. A 1 per cent solution of  $\text{MgSO}_4$  is recommended for intravenous injection in nephritic uremia to control the convulsions. It has a dehydrating effect on the brain (Blackfan). We attempted this in one case but stopped the injection because of the effect on the respiration.

It is the general belief that glucose solution if injected intravenously is burned, stored as glycogen and polymerized (Sansum and Woodyatt, and Erlanger and Woodyatt), and if the amount is greater than can be removed by these mechanisms, the excess is excreted in the urine, resulting in a polyuria. Therefore, our purpose was to give enough glucose to produce a glycosuria, thus hoping to initiate a diuresis. We found that in the normal individual 500 c.c. of a 20 per cent solution of glucose (100 gm.) if given over a period of sixty to ninety minutes will not produce a glycosuria; but if given in thirty to fifty minutes will result in 10 to 30 gm. being excreted in the urine. If 200 gm. of glucose are given in thirty to fifty minutes, from 70 to 100 or more grams will be excreted in the urine. We give the eclamptic patient 1000 c.c. of a 20 per cent glucose solution (200 gm.) intravenously over a period of thirty to fifty minutes, two, three, and sometimes four times daily. Twenty-four-hour urine examinations have shown that comparatively little or no glucose is excreted in the urine. In Table VI, we have tabulated those patients in whom we have twenty-four-hour urines and in only three cases was more than 100 gm. of glucose excreted in the urine per day. Two patients, Cases 3437 and 3380, received injections of

800 c.c. of a 30 per cent instead of 1000 c.c. of a 20 per cent solution, and the excessive glycosuria is apparently due to too great a strain on the tolerance which is apparently approximately 200 gm. We have decreased the amount of 30 per cent to 700 c.c., for although 30 per cent produces a more marked diuresis than 20 per cent, more sugar is excreted in the urine and apparently less toxic material excreted; for it seemed to us that these two cases did not respond as well to injections of 30 per cent as they did to 20 per cent. The glycosuria in the majority of the cases varied from none up to 50 gm. per twenty-four hours. There is no apparent relation between tolerance and weight or edema.

The urine output was increased in all cases to whom the treatment as detailed was given; but it was not due to the glycosuria for either there was none or at most of only a moderate degree. In the latter event the excretion of glucose is so small in proportion to the urine that it is evident that other factors are involved. Once a polyuria has been produced in eclampsia by glucose, it usually continues. This may be due to changes produced by the glucose in the cell or the cell membrane which are changed in pregnancy.

The blood pressure undoubtedly plays a part in the diuresis. Experimentally it has been proved that the urine varies directly as the blood pressure, therefore, in the eclamptics one would expect large amounts of urine but actually an oliguria or anuria exists. The fact that a diuresis can be established so rapidly with glucose indicates that the urinary suppression is due more likely to spasm of the renal capillaries rather than to edema of the kidney. Examination of the capillaries of the nail bed has shown that the circulation improves during glucose administration. In some cases, we have seen the beading disappear. Furthermore, when the serum proteins are high, the osmotic pressure exerted by them in the kidney holds water in the capillaries; but when they are low diuresis is apt to occur. Therefore, in eclampsia after delivery if the capillary spasm could be relieved, a marked diuresis should occur, for the blood pressure is high, the proteins are low and the water content of the blood is increased. A negative water balance after delivery in eclampsia with a urine output of 4 to 5 or even 6 liters is common. Another factor is the increase in  $P_H$  which increases the base binding property of the serum proteins and also increases their water binding power.

In eclampsia we find that after glucose injection the chlorides are increased in the urine, and since they are an electrolyte, they will exert a greater osmotic pressure than glucose, thus resulting in a greater diuresis. Their excretion indicates that the kidney is attempting to maintain the osmotic equilibrium of the plasma and since the blood sugar is being constantly increased, this can probably be accomplished more easily by excreting chlorides, which exert a greater

osmotic pressure than glucose. A gram of NaCl will exert slightly more than five times as much osmotic pressure as a gram of glucose.

Cushny states that glucose diuresis resembles that of urea in most points and may be accounted for in the same way by the failure of the epithelium of the tubule to take up the excess of sugar and its inability to absorb water against the osmotic pressure of sugar. He finds that following the injection of intravenous glucose, the concentration of sugar in the urine rises continuously while the chloride falls, especially during the ebb of diuresis. At this stage, therefore, the sugar is falling in the blood and rising in concentration in the urine, while the chloride is not changing in the blood but is falling in the urine. He states that apparently the glucose penetrates into the tissues and displaces the salt. In our studies, both in normal nonpregnant, normal pregnant and in eclamptics, we find that glucose does replace serum chloride. Table VII represents the changes produced in the blood and urine in a normal 87-kilo male by 500 c.c. of 20 per cent glucose solution (100 gm.) injected intravenously over a period of thirty-one minutes. There were no ill effects noted.  $\Delta$ , the depression of the freezing point of the serum, remained fairly constant, thus indicating a constant osmotic pressure of the serum. Therefore, the increased molecular concentration of the glucose was compensated for by a reduction in the electrolytes. Unfortunately we followed only the serum chlorides but with only these we find that the decrease in osmolar concentration of the chlorides followed closely the increase in glucose. However, one hour after the injection all findings were similar to those before the injection. In the toxemic and especially the eclamptic patient this is not true. Table VIII contains data obtained from a case of nephritis following a salvarsan injection. The patient was given 500 c.c. of a 20 per cent solution of glucose over a period of thirty-three minutes. A more marked reduction of chlorides occurred than in W. J. D. The cell volume returned to normal but the serum proteins remained below their initial reading. Table IX contains data obtained from an eclamptic patient who received 1000 c.c. of a 20 per cent solution of glucose (200 gm.) over a period of thirty minutes. Here again the chlorides showed marked reduction. The cell volume returned to its initial reading; but the proteins remained low. Thus the effect produced on the serum proteins especially but also on the blood as a whole by intravenous injections of glucose solution is similar to delivery, and in the mild case often initiates a cure of the disease; while in the severe it is palliative until delivery or fetal death occurs.

It has been known for a long time that in pregnancy there is a storage of chloride more likely due to the retention of water with a resultant retention of salt than to failure of the kidneys to excrete chloride, although in the pregnant sheep there is a definite retention of NaCl. (Lundin and Scharf.) In eclampsia this storage is markedly increased

even though there is no marked edema and the early convulsions in the majority of cases are, we believe, due to an edema of the brain which thus explains our control of convulsions with the glucose. We have found that the urine from eclamptics on admission, although concentrated as a rule, is relatively low in chlorides but after delivery or the death of the fetus the chloride concentration increases despite the diuresis which occurs. In the normal individual as the urine becomes more dilute the concentration of chloride decreases, but in the toxemias the reverse is true, and we have been able to cause marked excretions of chlorides in the urine by injecting glucose. In Table X we present data from a case of toxemia of pregnancy. The patient was admitted on August 17, 1928, because of headache and edema of the feet. The blood pressure was 215/120 and the urine contained a faint trace of albumin. On the seventeenth, eighteenth, nineteenth, and twentieth the amount of urine and chloride content varied but was in accord while the concentration was inversely proportional to the amount which is normal. Following the injection of 800 c.c. of a 30 per cent solution of glucose not only was the amount of urine and chloride increased but likewise the concentration of NaCl. This phenomenon occurred on each day that glucose was given. On the twenty-third and twenty-sixth no glucose was given and although the volume of urine remained high the chloride excretion was low. This decrease in chloride content after the washing out by glucose is due to retention by the body to replace tissue chloride. Since glucose replaces electrolyte, especially chloride, in the normal individual both in the blood and tissues, it is evident why the eclamptic patient with a tissue chloride retention will have a greater tolerance for glucose since the replacement is apparently based on the relative osmotic pressure exerted by chloride and glucose and not on their respective molecular concentrations. In some diabetic patients, Peters and coworkers find low serum chlorides and infer that the tissues are likewise deficient in chloride. Experimentally it has been demonstrated that there is an inverse relationship between the concentration of glucose and chloride in the blood after the injection of glucose, and it has been suggested that the chlorides possess the property of shifting to other tissues from the blood in order to preserve the optimal osmotic conditions in the blood (Foshay, Herrick).

A study of our cases has proved that the mild cases recover irrespective of the treatment, providing it is of a conservative nature, but in the severe type recovery is markedly favored by early death of the fetus or delivery. Since the blood dilution with its accompanying phenomena occurs after delivery or after death of the fetus, it is considered of prognostic value. Thus, for example, if, after the patient has been in our hands for eight to twelve hours and has been treated

as outlined, we find that the blood is not diluting, that there is no satisfactory diuresis, that coma is either not clearing up or is developing and that the temperature and pulse are increasing, then it is evident that the case is not only a severe one but delivery must be completed within a short period of time without additional shock. If delivery cannot be completed through the natural passage readily, then we prefer abdominal cesarean section under local anesthesia.

Table XI is self-explanatory. Our series is small but it has been carefully culled. A number of cases in whom the occurrence of convulsions was reported were excluded if the laboratory findings and subsequent clinical course were normal. (None of these died.) In the mild type one would expect no maternal mortality. In the severe type there will always be some maternal mortality and a high fetal mortality.

# CASE HISTORIES

TABLE II. M. W. 1760

DAY	CELL VOL.	SERUM PROTEIN PER CENT	GLUCOSE GM.		URINE C.C.	NaCl GM.	NaCl PER CENT	WEIGHT KILO.
			INTRAVENOUS	URINE				
4-10	41.6	6.4						166
11	46	5.68	385					Delivery
12	27	4.43	200 (11 and 12)	22	7200	12.3	0.17	
13				13	2000	13.2	0.66	
14	28	4.92		0	4000	20.4	0.51	
15			90	0	5100	26.5	0.52	
16				0	4300	15.9	0.37	130
17	30	5.7		0	5500	21.4	0.39	
18					4000	26.8	0.67	
19	30.6	5.38			1400	7.1	0.51	
20					2500	7.3	0.27	
21					3900	9.4	0.24	
22					3000	8.4	0.28	
23	32	6.45			3100	6.2	0.205	121
24					2900	7.85	0.27	
25					2700	8.35	0.31	
26					2300	6.45	0.28	
27	36	7.05			2100	5.65	0.27	120
28					2150	5.57	0.26	
29					1500	4.5	0.30	
30					2600	7.28	0.28	
5- 5	36	7.23						116

M. W., 1760, primipara, thirty-four years old. At term. On April 6, 1928 patient had two convulsions and on April 10 she had four more. Admitted to hospital on April 10, 1928. She was very obese, in coma, and had a general edema. Blood pressure was 230/140. Urine coagulated on heating. During a period of fifteen hours the patient received 385 gm. of glucose intravenously and voided 1100 c.c. She became conscious. In view of the duration of the disease and the fact that the patient was now in the best condition that could be expected, a cesarean section under local anesthesia was done. A living 5110 gm. baby was delivered. Discharged on May 4, 1928. Note: The decrease of serum proteins before delivery. Marked blood dilution, diuresis, and weight loss (50 kilo in three weeks) after delivery.

TABLE III. E. A. 3380

DAY	CELL	SERUM	GLUCOSE GM.		URINE C.C.	NaCl GM.	NaCl PER CENT	WEIGHT KILO.
	VOL. PER CENT	PROTEIN PER CENT	INTRAVENOUS	URINE				
10-18	45	5.55	440	120	2000	1.8	0.09	165
19	49	5.52	880	154	3350	5.3	0.16	Delivery
20	41	4.15	396	98	3060	5.8	0.19	
21	40	4.26	420	239	3810	7.7	0.20	
22	34	4.85	480	126	3450	6.5	0.19	
23	39.5	4.82	430	155	3250	5.8	0.18	
24				0	1300	0.7	0.05	
25				0	2075	0.5	0.02	
26	30	5.15		0	3250	1.0	0.03	
30	24.5	5.1						
11-5	35	6.26						

E. A., 3380, primipara, sixteen years old. Forty-one weeks gestation. Normal pregnancy. Admitted on October 18, 1928. Had had headaches and dizziness for past two days. Blood pressure 142/75. Edema of ankles and face. Urine contained a large amount of albumin. Phenolsulphonephthalein test, 70 per cent in two hours with total urine output of 550 c.c. Four hours after admission patient had a convulsion and blood pressure rose to 170/110. During the next fifteen hours she had three more convulsions but despite 42 c.c. of 25 per cent  $MgSO_4$  solution given during this period together with 2000 c.c. of 20 per cent and 800 c.c. of 30 per cent glucose solution intravenously, patient gradually became comatose, with temperature rising to  $39.8^\circ C.$  and pulse to 132. Patient was having contractions and the cervix admitted 1 finger, but delivery from below could not be completed under twelve to eighteen hours at a minimum, therefore, a cesarean section under local anesthesia was performed. A living 3450 gm. baby was delivered. Discharged November 9, 1928. Note: The steadily increasing blood concentration despite treatment. Marked dilution and diuresis after operation.

TABLE IV. W. P. 2734

DAY	CELL	SERUM	GLUCOSE GM.		URINE C.C.	NaCl GM.	NaCl PER CENT	WEIGHT KILO.
	VOL. PER CENT	PROTEIN PER CENT	INTRAVENOUS	URINE				
8-12	34	5.13	400	7	500	0.85	0.17	
13	32.6	4.5	350	29	1650	0.93	0.06	
14			200		700			71
15				0	400	0.14	0.035	
16				0	500	0.01	0.002	
17	31.6	4.69		0	1630	0.23	0.014	72
18	55.2	5.60	100	12			0.006	
19	46	4.94	350	0	600	0.04	0.006	Delivery
20	32	4.28		0	5900	2.71	0.046	
21				0	5150	10.3	0.2	
22				0	5300	20.14	0.38	60
23				0	3800	13.4	0.35	
24	32	5.28		0	1600	4.4	0.276	

W. P., 2734, primipara, nineteen years old, thirty-six weeks gestation. Admitted on Aug. 12, 1928 on account of headache, edema of ankles and blood pressure of 180/110. Urine coagulated on heating. Received 1000 c.c. of 20 per cent glucose solution intravenously once or twice daily. Phenolsulphonephthalein test on Aug.

17, 1928 was 25 per cent for two hours. Despite treatment the urine output steadily decreased, blood pressure remained high, and headaches became more frequent. Patient had a Braun bag inserted on August 19 and after a twenty-five hour labor was delivered by perineal forceps of a living 2360 gm. baby. During labor the patient had one convulsion but was not delivered until twelve hours later. On August 31, P.S.P. was 70 per cent for two hours. Discharged on Sept. 1, 1928. Note: The blood dilution on admission which became concentrated at time of convulsion. Oliguria developing while under treatment and almost *complete disappearance of chloride from the urine*, associated with a rapid gain in weight. Marked diuresis postpartum during blood dilution phase, with relatively high concentration of urine chloride.

TABLE V. F. F. 11738

DAY	CELL VOL. PER CENT	SERUM PROTEIN PER CENT	GLUCOSE GM.		URINE C.C.	NaCl GM.	NaCl PER CENT	WEIGHT KILO.
			INTRA "V"	URINE				
7-18	46.4	6.0	575		600			77.6
19	34	3.82	200	7	900	1.0	0.011	
20	34	3.89	400	1	400	0.2	0.058	Death of fetus
21	34.6			0	2400			
22				0	4000	2.0	0.053	
23				0	6600	7.3	0.110	
24				0	5400	6.4	0.119	
25	36	4.71		0	1300	3.7	0.140	
26				0	1300	2.2	0.168	
8- 3	31.8							
8-17	40	6.35						62.5

F. F., 11738, primipara, seventeen years old, thirty-six weeks gestation. Edema of ankles for past week. Headache and dizziness for past twelve hours. Admitted on July 18, 1927, having already had 2 convulsions. Blood pressure 180/120. Marked edema of feet and legs. Urine coagulated on heating. Patient had 2 more convulsions during first four hours in hospital. No fetal movements were noted by the patient after July 20. On July 21, the P.S.P. was 70 per cent for a two hour total. On July 25 bougies were inserted and after an eighteen hour labor a macerated 2130 gm. baby was delivered. Discharged Aug. 17, 1927. Note: The blood concentration on admission and the marked dilution which occurred twenty-four hours later before death or delivery of the fetus. The protein dropped 36.7 per cent and the cell volume 27 per cent. A marked diuresis together with increasing concentration of urine chlorides occurred after death of the fetus.

#### CASE HISTORIES OF PATIENTS WHO DIED

A. K., 5365, gravida v, twenty-nine years old, twenty-four weeks gestation. Over a period of two months had had attacks of epigastric pain and vomiting. On Jan. 14, 1924 had similar attack and began to have convulsions. Admitted on Jan. 15, 1924. Deep coma. Temperature 39.8° C. Pulse 144. Respiration 46. Blood pressure 140/?. Urine coagulated on heating. During the twelve hours before death patient received approximately 5000 c.c. of fluid together with stimulants. No urine obtained after initial specimen. Autopsy Diagnosis: Eclampsia. Acute tubular nephritis. This patient was considered moribund on admission because of irregular, rapid, thready pulse, anuria, duration of the disease and the deep coma. The liver was almost completely destroyed by hemorrhage and necrosis.

S. L., 7315, primipara, twenty-six years old, thirty six weeks gestation. Edema of legs for month. Headache, spots before eyes, pain in epigastrium for last four days. Had 2 convulsions before admission on Oct. 16, 1926. She was in deep coma and very edematous. Urine contained large amount of albumin. Blood pressure 180/125. Had one convulsion shortly after admission. Within twenty-four hours following treatment the patient was conscious and fully coordinated. On October 18 patient began to vomit and abdomen became distended. Blood pressure had risen to 210/135. Urine output on eighteenth was 930 c.c., on nineteenth was 2775, on twentieth was 1800 and on the twenty-first was 1050. On the nineteenth approximately 550 c.c. of blood were removed. On the nineteenth, patient

TABLE VI

NUMBER	WEIGHT	EDEMA	DAY	GLUCOSE GM.		URINE C.C.
	KILO.			INTRA "V"	URINE	
M. W. 8392	87.9	Ankles	22	400	19	720
			23	500	28	4900
			24	400	28	4040
			25	200	12	2420
			26	200	0	1800
	78.2	27	200	0	2650	
F. F. 11,738	77.6	Legs	18	575		600
	76		19	200	7	900
	62.5		20	400	1	400
E. B. 440	70.2	General	16	400	1	830
			17	750	32	3100
			18	200	57	4500
N. C. 1332	78.9	Ankles	16	320	23	1400
			17	100	0	2500
			18	100	0	4000
	67.5	19	200	0	2100	
M. W. 1760	166	General	11-12	585	22	7200
	116		13		13	2000
	14		200	0	4000	
	15		90	0	5100	
W. P. 2734	71	Legs	12	200	7	500
	72.3		13	350	29	1650
	60		14	200	0	700
	18		200	0	400	
	19		150	12	500	
L. W. 4129	72	General	17	290	35	1500
	49.5		18	180	36	2000
	47		19	240	65	1600
W. B. 4640	69	Ankles	2	500	9	1775
	61.8		3	200	62	500
			4		10	1700
F. S. 3779	69.6	Ankles	6	400	77	2950
			7	370	120	2850
			8	200		3650
W. W. 3437	65	Ankles	25	400	58	1310
			26	400	118	2100
			27	480	91	2400
	58.2	28		68	2600	
E. A. 3380	75	Ankles	18	440	120	2000
			19	880	154	3350
			20	400	98	3060
			21	420	239	3810
			22	480	126	3450
			23	440	155	3250



became incoordinated and finally unconscious with a temperature of 38.4° C. and pulse of 150. On the twentieth, a Voorhees bag was inserted and the fetus delivered after a twelve hour labor. Death occurred on October 21, apparently of pulmonary embolism. Patient should have been delivered on the seventeenth, when the maximum improvement had occurred.

TABLE VII. W. J. D.

TIME	CELL	SERUM	PLASMA	PLASMA	Δ	GLUCOSE GM.		URINE	NaCl	NaCl
	VOL.	PROTEIN	NaCl	B.S.		INTRA	"V" URINE			
	PER	PER	MG.	MG.				C.C.	GM.	PER
	CENT	CENT								CENT
0	48.5	7.38	586	97	0.544	100 gm.		110	1.06	0.96
15 min.	44	6.13	573	450	0.532					
30 min.	42	5.53	555	550	0.56					
1 hr.							11	358	1.32	0.34
1 hr. 40 min.	48	7.28	590	159	0.546					
2 hr.							4	230	0.49	0.21
3 hr.							0.1	25	0.25	1.0

TABLE VIII. A. II. 2329

TIME	CELL VOL. PER CENT	SERUM PROTEIN PER CENT	PLASMA NaCl MG./100 C.C.	PLASMA B. S. MG./100 C.C.	GLUCOSE INTRA "V" MG./100 C.C.
0	39	6.47	585	92	100 gm.
12 min.	34	5.4	545	565	
33 min.	32.7	5.2	508	690	
1 hr. 35 min.	36.3	6.06	600	195	

TABLE IX. M. B. 4640

TIME	CELL VOL. PER CENT	SERUM PROTEIN PER CENT	PLASMA NaCl MG./100 C.C.	PLASMA B. S. MG./100 C.C.	GLUCOSE INTRA "V" MG./100 C.C.
4-28 A.M.	40	7.47	619	108	200 gm.
15 min.	36	5.75	554	590	
33 min.	34.5	5.1	548	912	
1 hr. 43 min.	39.5	6.4	566		
4 hr. 13 min.	41	6.62	578		
9 hr.	40	6.6	566		
4-3 A.M.	30	5.38	579	82	
4-4 A.M.	27	5.65	531	77	

M. B., 4640, primipara, thirty-nine weeks gestation. Admitted on March 31, 1929. Blood pressure 130/80. On April 2 after patient had been in labor for twenty-four hours with low fluid intake and output, she had a convulsion with blood pressure of 170/115. Delivery was completed nine hours later by perineal forceps. Baby was living and weighed 3165 gm. Discharged April 22, 1929. Classified as mild. Note: Following the glucose injection, the serum protein dropped and remained low although the cell volume returned to its initial reading until after delivery. Marked drop in plasma chlorides during glucose injection.

TABLE X. O. H. 2796

DAY	GLUCOSE GM.		URINE C.C.	NaCl PER CENT	NaCl GM.
	INTRAVENOUS	URINE			
17		0	1240	0.4	5.0
18		0	2200	0.2	4.4
19		0	1850	0.26	4.8
20		0	1700	0.26	4.4
21		0	2900	0.19	5.5
22	225	61	3400	0.27	9.2
23		0	2525	0.07	1.8
24	225	74	3300	0.15	5.0
25	270	64	3250	0.14	4.6
26		0	2300	0.056	1.3
27	270	75	3400	0.16	5.4

TABLE XI. CASES OF ECLAMPSIA, 1923-1929

CASES	NUMBER	POST- PARTUM	SPONTA- NEOUS ONSET OF LABOR	INDUC- TION OF LABOR	CESAREAN SECTION	MATERNAL MORTALITY	BABY	
							LIVING	DEAD
Mild	15	6	8	1	1		15	
Severe	18		7	4	4	3 (2 undelivered)	10	6 misc.
Total	33	6	15	5	5	3	25	6

W. H., 3283, gravida ii, thirty-five years old, twenty-eight weeks gestation. Admitted as a private patient on Oct. 8, 1928 at 8 A.M. because of vomiting and loss of consciousness. Onset was about eight hours before admission. Shortly after entry she had a convulsion. Blood pressure was 195/105 and a slight edema existed. Urine coagulated on heating. Therapy consisted of 500 c.c. of 20 per cent glucose solution intravenously, 1000 c.c. of Ringer's solution subpectorally and 10 c.c. of a 25 per cent solution of  $MgSO_4$  at 11 A.M. At 4 P.M. 800 c.c. of urine were obtained by catheter. At 7 P.M. patient was given 250 c.c. of a 20 per cent glucose solution intravenously and 1000 c.c. Ringer's subpectorally. At 9 P.M. 300 c.c. of blood were removed. Stimulants were started at this time. At 10 P.M. 250 c.c. of urine were obtained by catheter, 11 P.M. venesection of 500 c.c. of blood, 11:45 P.M. patient given glucose and 450 c.c. citrated blood. Stimulants continued. Respiration gradually increased until the rate was 40 to 50 per minute. Death occurred at 8 A.M., twenty-four hours after admission. Autopsy Diagnosis: Eclampsia. Focal necrosis of liver. Degeneration of the kidneys. The ease with which a diuresis was established with the small amounts of fluid, the early admission to the hospital after the onset together with the duration during which the patient was treated warrant the belief that more intensive use of hypertonic glucose solution and delivery in the afternoon would probably have resulted in recovery.

## SUMMARY

Eclampsia is best treated by certain definite procedures which by their success or failure permit one to note the progress of the case. After delivery or death of the fetus a marked blood dilution takes place, during which period a diuresis occurs. Clinical improvement is closely associated with these phenomena. The eclamptic patient has an increased tolerance for glucose, probably due to the retention of chlorides found in pregnancy. The injection of large amounts of intra-

venous glucose solution will simulate temporarily at least the effect produced by delivery. The prognosis for the patient with a severe type of eclampsia is chiefly favored by delivery or early fetal death.

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630 SOUTH KINGSHIGHWAY.

### THE KIDNEY OF PREGNANCY\*

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THE purpose of the paper is to summarize and coordinate our present knowledge of the kidney of pregnancy, and to present certain additional information. The title is used in a broad sense to include the following study:

1. The diagnosis of hydronephrosis, infected hydronephrosis, and pyelitis complicating pregnancy, with a comparison of the relative frequency of appendicitis and gall bladder disease.

2. The relation of hydronephrosis and pyelitis to early and to late gestational toxemia.

3. Differential kidney function tests and pyelograms to discover additional factors in the cause of the common hydronephrosis of pregnancy, with special attention to the possibility of ureteral edema or chronic passive congestion, that might be a contributing cause to late gestational toxemia and eclampsia.

4. An attempt to differentiate renal and hepatic toxemia of pregnancy by the effect of heparmone administration.

Our study therefore contains a review of over seventy leading articles, not only on the above subjects but also on the newer aspects of renal and hepatic function, and the classification of gestational toxemias. The second part contains tables and illustrations from our experience from May 1, 1926, to May 1, 1929, with the behavior of the kid-

\*Read by invitation.

ney of pregnancy. For ten years I have had charge of the cystoscopic work in the Department of Obstetrics of the Hospital of the University of Pennsylvania, through the courtesy of the Professor of Obstetrics, first, Dr. Barton C. Hirst, later, Dr. Edmund B. Piper. This arrangement of having one member of the regular Obstetric Staff responsible for the usual urologic complications of pregnancy and the puerperium is an eminently satisfactory one, conducive to proper interest in and to accurate diagnosis of diseases of the maternal urinary tract, without which plan such records as herein given would be impossible.

A summary of the literature as mentioned will not review the pathologic histology of the renal and hepatic parenchyma in the toxemias, including eclampsia, except to mention the description of Schwarz<sup>1</sup> and of Dieckmann,<sup>2</sup> but rather the function and infection of the upper urinary tract, and hepatic function.

In Europe, the urea kidney function tests<sup>3-5</sup> including Ambard's constant, appear to be favored, on the grounds of better estimation of renal reserve, but such tests are technically difficult, and in cystoscopic differential studies they require occluding catheters. Therefore the dye tests, notably indigocarmine, are favored in this country. None of these, nor any urinary findings<sup>6</sup> of the present day alone, will designate a clear-cut type of late gestational toxemia, although there is hope that identification of liver protein in the blood or urine of sensitized rabbits may eventually prove the diagnosis of hepatic toxemia, if there be such an entity.

Neither do routine blood chemistry tests<sup>10</sup> assist to any degree in differentiating renal from hepatic insufficiency in pregnancy. In the University Maternity Hospital during the period of three years from May 1, 1926, prenatal patients with toxemia symptoms or blood pressure over 150 systolic, as well as other toxemic patients, have had careful check of blood urea nitrogen, uric acid, creatinin, blood sugar, CO<sub>2</sub> and Van den Bergh tests, yielding no curve that could be plotted for diagnostic or prognostic significance, except in extreme cases. We recognize, however, a low CO<sub>2</sub>-combining power of the blood as a menace requiring alkalization (Wilson), and appreciate the value of morphine and luminal, glucose, magnesium sulphate, vapor baths, etc., for nearly all types of eclampsia.

The nearest approach to division of the late toxemias may be made by utilization of simple laboratory tests and clinical manifestations,<sup>11</sup> especially blood pressure,<sup>12</sup> eyegrounds, urinary specific gravity, edema, progress of symptoms, and recovery up to six to twelve weeks postpartum. The simple differentiation that we have been teaching students for several years, amplified by Mussey and Keith,<sup>13</sup> is briefly as follows:

A. Acute late gestational toxemia characterized by rapid onset late in pregnancy, with good dye elimination, high urinary specific gravity, and complete recovery within three months of delivery.

B. Chronic late gestational toxemia featured by gradual onset, earlier in pregnancy, frequently as an exacerbation of prior hypertension, often seen in multip-

arae; poor dye elimination, marked eyeground changes, low urinary specific gravity, and incomplete recovery in three months.

Definitions of gestational toxemia, such as preeclamptic, mild, severe, etc., are confusing and have been discarded in our tables in favor of the classification just mentioned. We have not attempted to divide our patients into hepatic toxemias,<sup>11-20</sup> on the basis of liver function tests. Some years ago several of our cases of generalized pruritus complicating pregnancy showed abnormal retention of phenoltetrachlorophtha-



Fig. 1.—Infected hydronephrosis (35 c.c.) and ureteral edema associated with mild toxemia of late pregnancy. Absence of obstruction and lateral deviation of ureter permitted prompt relief by raising foot of bed. Proof of circulatory cause of impaired ureteral drainage.

lein,<sup>21</sup> but a small series of so-called hepatic type toxemias failed to demonstrate constant retention of this dye, so that we are unable to depend upon the test in this connection, in spite of the well-known tendency of pregnancy toward hypercholesterolemia, gall bladder disease, and hepatic degeneration.

Finally in regard to ureteropelvic dilatation and infection, it was inevitable that proof in vivo of extreme frequency in puerperal women, would follow postmortem evidence,<sup>22</sup> such proof having been estab-

lished in numerous articles.<sup>27-28</sup> Close association with late toxemia has also been shown, and lately etiologic factors in the production of the above conditions, which Kretschmer and Heaney<sup>29</sup> were among the first to visualize by pyelography. Most followers attempted to explain ureteropelvic distortion by actual pressure of the gravid uterus,<sup>30-40</sup> increased intra-abdominal tension, stricture,<sup>41</sup> infection,<sup>42-45</sup> and other causes,<sup>47-49</sup> but Hofbauer<sup>50</sup> by a study of morbid anatomy demonstrated the most important factors to consist of hyperplastic and hypertrophic changes in



Fig. 2.—The kidney of pregnancy. Lateral deviation of ureter with low grade infection of moderate hydronephrosis (22 c.c.) and typical hydroureter complicating late pregnancy.

the pelvic portion of the ureter including musculature, connective tissue, and sheath, producing a narrow lumen at this point. The latter author also stressed the action of increased bile acid in the mother's blood in reducing uterine, intestinal, and ureteral muscular contraction. Hofbauer's discovery may not quite agree with the very recent report of Frater and Braasch<sup>51</sup> from the ureteral study of 93 autopsies, nearly half of which were women, some pregnant, and some having borne children, in which they found only four abnormal ureteral narrowings, of which two were noninflammatory strictures, one congenital narrowing,

and one extraureteral growth. Atonic dilatation without stricture due to infection was also demonstrated.

Duncan and Seng<sup>52</sup> have contributed invaluable information by proving that many apparently normal pregnancies show latent ureteral infection usually with coliform organisms, atonic dilatation (hypertrophy), and delayed emptying of the ureter, all of which can readily predispose to a toxemic state. The work of Traut,<sup>53</sup> of Morrison<sup>54</sup> on the routes of absorption in hydronephrosis by experimentation with dyes in totally obstructed ureters, and Ferrer's<sup>55</sup> report of obstruction to venous circulation in the kidney caused by distention of the pelvis and



Fig. 3.—Persistence of hydronephrosis, and ureteral kink in same patient thirteen days after delivery. Same result with sterile urine four weeks later.

calices, also bear on the subject of our paper, the first two denoting a guide to possible damage by careless pyelography. These studies support one conclusion from our own observations that late gestational toxemia is for the most part primarily of renal origin, and would explain the report of FitzHugh<sup>56</sup> on the urohepatic syndrome or interrelation of renal and hepatic pathology.

The infrequency of appendicitis, once in 525 pregnancies, suggests a connection between chronic appendicitis and sterility. On the other hand, the remarkable frequency of pyelitis or infected hydronephrosis,

once in 15 pregnancies, contrasts with the report of another Philadelphia Maternity Hospital for one year, giving only 8 or 10 cases of pyelitis in about 1000 pregnancies, the difference being due to method of diagnosis.

TABLE I. FROM THE DEPARTMENT OF OBSTETRICS, HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

Total pregnancy admissions from 5/1/26 to 5/1/29	2101
Pyelitis and infected hydronephrosis	140
Simple hydronephrosis (severe)	23
Gall bladder disease	12
Appendicitis	4
Early gestational toxemia	44
Late gestational toxemia and eclampsia	232

TABLE II. PYELITIS AND INFECTED HYDRONEPHROSIS (POSITIVE CULTURE, PUS, OR FEBRILE WITH SYMPTOMS)

Total number				140
Primiparae	right 39	left 7	bilateral 24	
Multiparae	" 30	" 12	" 28	
Infesting organisms (total cases with positive culture)				26
Coliform				19
Other organisms				7
Onset during pregnancy				116
History of prior urologic disease				24
Medical treatment				82
a. Relapse				4
b. Persisted at follow-up				8
Cystoscopic treatment				58
a. Relapse				2
b. Persisted at follow-up				4
Total cases of:				
Early gestational toxemia				44
Accompanied by pyelitis (active)				3
Vomiting relieved by cystoscopy				1
Late gestational toxemia and eclampsia				232
Accompanied by pyelitis (active)				16
(See tables IV, V, VI.)				

Noticeable is the comparatively small number of positive cultures from pyelitis (26 out of 58 cystoscopies). Our technic may account for this. This is carried out as follows:

All patients are examined under similar conditions as far as possible, that is, at about the same time of the clinic day, without morphine, and after two glasses of water. No. 7 opaque catheters frequently renewed, boiled after use in infected cases, and always injected with and immersed in 4 per cent formalin solution are used, being flushed with sterile water just before introduction. All other apparatus is scrubbed; tables, etc., are prepared exactly as for a major operation, in a special cystoscopic room. Catheter specimens are examined by the William Pepper laboratory. Five c.c. of 0.4 per cent indigocarmine is injected intravenously before ureteropelvic distention is tested which is done after appearance of the dye. Twenty to 30 c.c. (or more) is injected in as many seconds, while the patient is questioned for pain and as the ureteral orifice is watched for blue tinted leakage. The amount of recovery during the time of injection is noted, and checked by many pyelograms, which in virtually all cases have confirmed the first injection.



Whereas early gestational toxemia was complicated in three cases by febrile pyelitis, silent infection of the kidney of pregnancy was present in several more, both primiparae and multiparae, suggesting unrecognized pyelitis in childhood on the part of the former, and persistent kidney of pregnancy of the latter.

Table III, showing an average ureteropelvic content of 15 to 18 c.c., means the minimum average before any leakage, with no pain on injection. In these cases, as in many of the infected hydronephroses, injec-



Fig. 4.—Infected hydronephrosis in primipara associated with hyperemesis gravidarum, with history of prior pyelitis. Each condition improved by ureteral lavage and drainage.

tion of the ureters could usually be done much more rapidly than with normal ureters, often to a surprising maximum of 30 to 50 c.c., denoting atonic dilatation. Several of the more pronounced unilateral hydronephroses showed a definite difference in the urinary specific gravity of the right and left kidneys.

Of the 44 early toxemic patients 7 primiparae less than eight weeks pregnant had cystoscopic examinations, only 2 of these showing any evidence of ureteropelvic dilatation.



Fig. 5.—Advanced infected hydronephrosis (over 35 c.c.) of pregnancy, probably from pyelitis in childhood. Note extreme lateral deviation and lengthening of ureters.

Fig. 6.—Moderate persistence of hydronephrosis in same patient, with ureteral kinking thirteen days after delivery.

Whenever the term severe hydronephrosis appears in this report, it denotes either marked ureteropelvic dilatation proved by cystoscopy and greater than the usual amount in pregnancy, or presumably the same condition designated by objective and subjective symptoms with negative bladder pus and culture.

The rather high figure of 151 in Group A, late gestational toxemias, may be accounted for by the mild degree of many cases which were admitted with moderate hypertension as the main symptom. Although the indigo carmine differential dye tests were fair in the cystoscoped Group B cases, other symptoms warranted such cases to be placed in this group along with many showing reduced phenolsulphonephthalein output. Emphasis on ureteral edema is made to bring up the connection between vasodilatation or circulatory stasis about the distal ureter with late gestational toxemia. Several instances encountered either in association with a very low fetal head, especially in early labor, marked varicosities of vulva, hypertrophic cervicitis, or subinvolved retroversio uteri, suggest this form of impaired ureteral drainage as a possible cause of certain cases of toxemia.

TABLE III. SIMPLE HYDRONEPHROSIS (NEGATIVE CULTURE, NO CLUMPING OF W.B.C., AFEBRILE)

Total, severe	23
Proved by cystoscopy	14
Primiparae	right 1      left 0      bilateral 3
Multiparae	“ 7      “ 0      “ 3
Average pelvieuireteral content (over)	15-18 c.c.
History of prior urologic disease	3
Stone	2
Stricture(?) (Not present at this time)	1
Onset during pregnancy	21
Cystoscopic treatment	14
Relapse	2
Persisted at follow-up	0
Early gestational toxemia	44
Accompanied by hydronephrosis (severe)	1
Vomiting relieved by cystoscopy	1
Late gestational toxemia and eclampsia	232
Accompanied by hydronephrosis (severe)	17
(See tables IV, V, VI.)	

The reason for the favorable dye tests in the 5 cystoscoped eclamptics can be explained by convalescence. One-third of the 23 eclamptics showed marked hydronephrosis or pyelitis. From 1915 to 1920 approximately 100 eclamptics were admitted to the University Maternity ward from various sources, of whom 14 died. From May 1, 1926, to May 1, 1929, 23 eclamptic patients were admitted, only 2 from our own prenatal division, of whom 3 died.

## UROLOGIC SUMMARY

Certain significant facts are brought out by a summary of the 97 obstetric patients subjected to urologic diagnosis by cystoscopy and pyelography:

1. Ureteral obstruction appeared only four times, in the form of calculus twice, congenital narrowing of the orifice and stricture. This absence of frequent obstruction presupposes some additional factor responsible for impaired drainage not accounted for by atonic ureteral dilatation or latent infection so common in pregnancy. This impairment we believe is circulatory in the form of intermittent

TABLE IV. LATE GESTATIONAL TOXEMIA

<i>A. Acute:</i> late pregnancy, rapid onset, high urinary specific gravity, good dye test, complete recovery in 6-12 weeks.				
Total cases				151
Accompanied by:				
Hydronephrosis (severe)				4
Pyelitis (active)				5
Cystoscoped:				
Hydronephrosis				4
Primiparae	right 2	left 0	bilateral 0	
Multiparae	" 1	" 0	" 1	
Indigocarmine diff. (average)				
Right 8 min., left 7 min.				
Evidence of ureteral edema corresponding with the hydronephrosis				3
Pyelitis				3
Primiparae	right 0	left 0	bilateral 2	
Multiparae	" 0	" 0	" 1	
Indigocarmine diff. (average)				
Right 5 min., left 7 min.				
Evidence of ureteral edema corresponding with the pyelitis				0

TABLE V. LATE GESTATIONAL TOXEMIA

<i>B. Chronic:</i> starting earlier in pregnancy, slow progress, older multiparae often, or prior hypertension, low urinary specific gravity, poor dye test, eyeground changes, poor recovery.				
Total cases				58
Accompanied by:				
Hydronephrosis (severe)				8
Pyelitis (active)				7
Cystoscoped:				
Hydronephrosis				7
Primiparae	right 1	left 0	bilateral 1	
Multiparae	" 3	" 1	" 1	
Indigocarmine diff. (average)				
Right 3 min., left 8 min.				
Evidence of ureteral edema corresponding with hydronephrosis				3
Pyelitis				5
Primiparae	right 0	left 1	bilateral 1	
Multiparae	" 0	" 0	" 3	
Indigocarmine diff. (average)				
Right 7 min., left 10 min.				
Evidence of ureteral edema corresponding with pyelitis				3

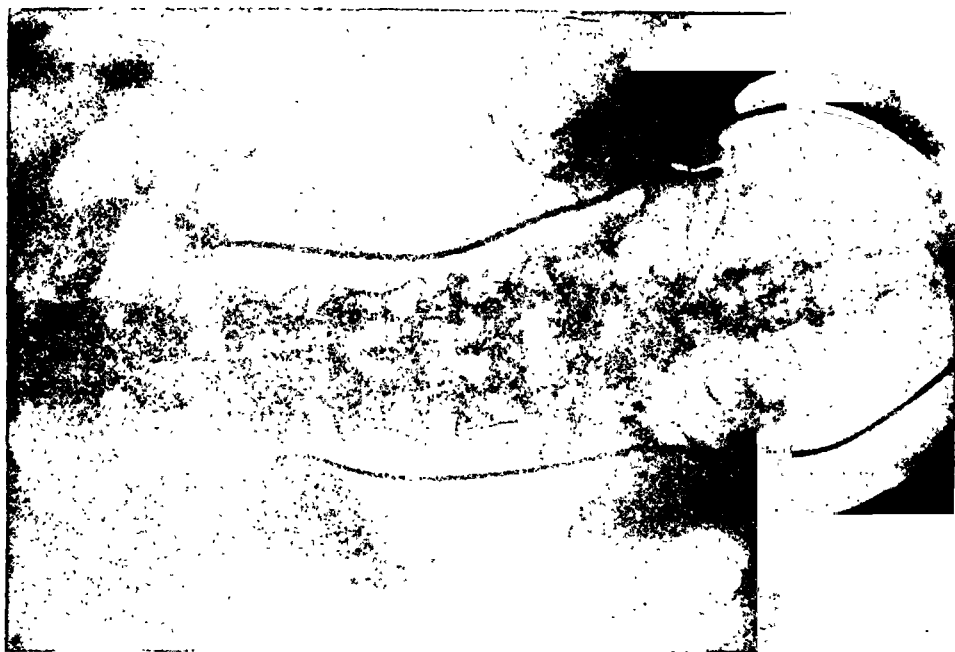


Fig. 8.—Bilateral nephropoiosis before pregnancy. Reclying.

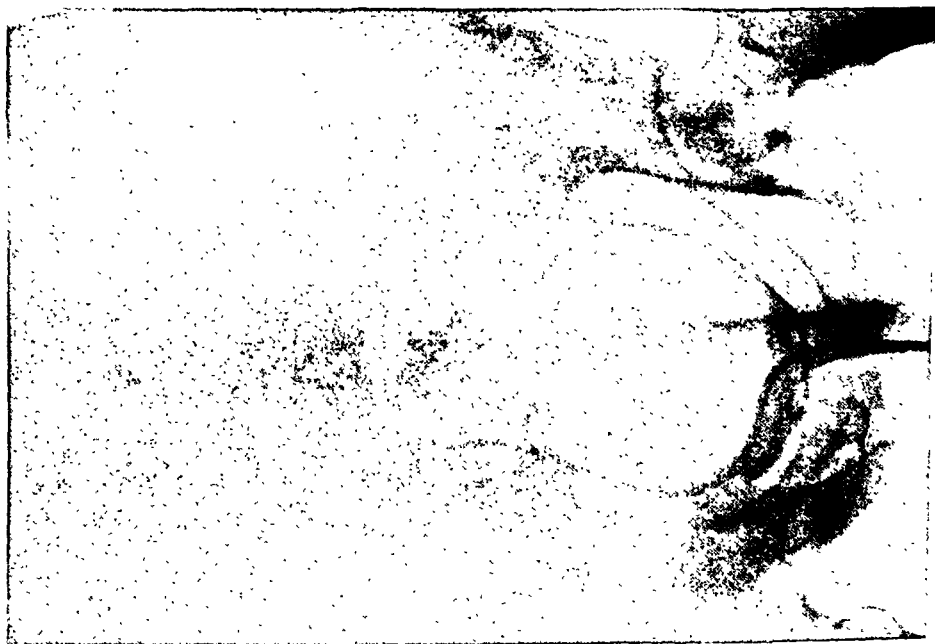


Fig. 7.—Bilateral infected ureteropelvic dilatation due to calculus six years before, associated with a seven months' pregnancy, without toxemia. Note course of right catheter. Normal appendix removed before admission.

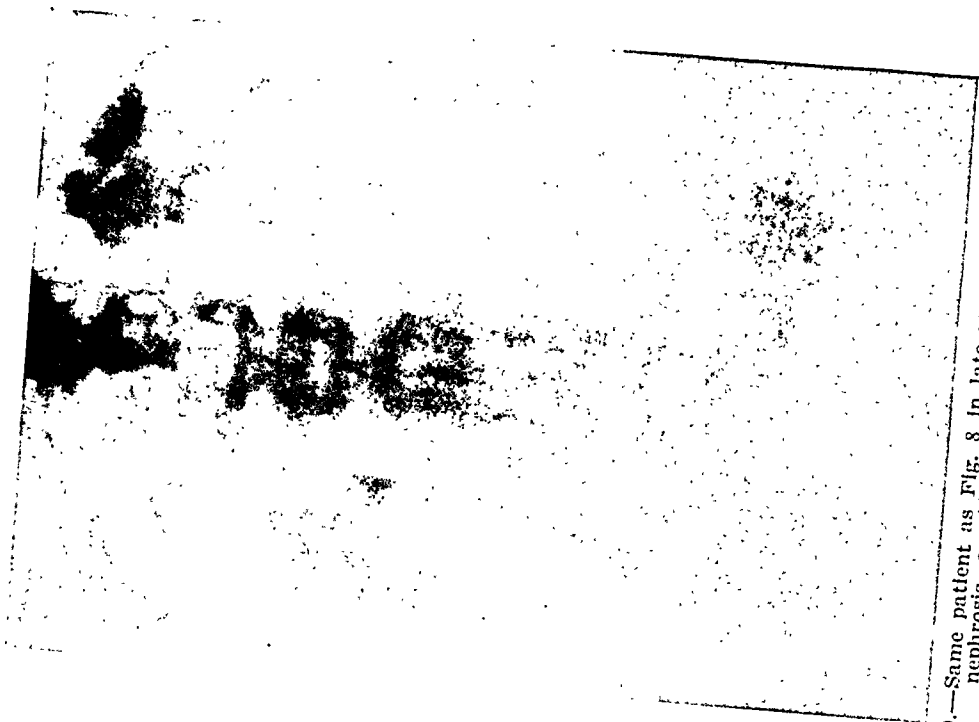


Fig. 10.—Same patient as Fig. 8 in late pregnancy. Moderate hydro-nephrosis, considerable pain, relieved by posture.



Fig. 9.—Sitting posture. Same patient as shown in Fig. 8.



Fig. 11.



Fig. 12.

Figs. 11 and 12.—Large calculus in right pelvis, and stricture of left ureter, with bilateral infection, six weeks after delivery. The effect of infected hydronephrosis beginning in pregnancy, and the cause of severe late gestational toxemia.

vasodilatation or chronic passive congestion of and around the distal ureter, evidenced by edema of the orifice in the form of irregularity of shape and puffing.

2. Jaundice did not appear in any case, but one instance of subacute exacerbation of a chronic cholecystitis followed ureteral catheterization. Therefore it appears that even if the renohepatic interrelation be of importance in infection and toxemia, it plays no great part in careful cystoscopy of the obstetric patient.

3. Other harmful results of urologic investigation included two troublesome increases in severity of chronic pyelitis, and one precipitation of labor at term.

TABLE VI. LATE GESTATIONAL TOXEMIA

C. Eclamptic Type (of Groups A and B) total	23
Group A. Acute	17
Accompanied by:	
Hydronephrosis (severe)	3
Pyelitis (active)	3
Cystoscoped:	
Hydronephrosis	2
Primipara right 0 left 1 bilateral 0	
Multipara " 0 " 0 " 1	
Indigocarmine diff. (average)	
Right 4½ min., left 3 min.	
Evidence of ureteral edema corresponding with the hydronephrosis	2
Pyelitis	2
Primipara right 0 left 1 bilateral 0	
Multipara " 0 " 0 " 1	
Indigocarmine diff. (average)	
Right 9½ min., left 8½ min.	
Evidence of ureteral edema corresponding with the pyelitis	2
Group B. Chronic	6
Accompanied by:	
Hydronephrosis (severe)	2
Pyelitis (active)	0
Cystoscoped:	
Hydronephrosis	1
Primipara none	
Multipara right 1 left 0 bilateral 0	
Indigocarmine diff.	
Right 20 min., left 4 min.	
Evidence of ureteral edema corresponding with the hydronephrosis	1

Heparhormone table (Table VIII) speaks for itself, but fails to mention the sudden headache so commonly produced by intravenous injection, which should be by slow drip or discarded in favor of intramuscular administration. No dangerous reactions occurred, but also no marked symptomatic improvement was maintained after injections were stopped, with one brilliant exception where heparhormone alone cured a very ill woman.

The 27 cases were reported on toxemia record forms provided by the Committee on Toxemia of the Philadelphia Obstetrical Society. Dr. Woodward of the Eli Lilly Research Department very kindly furnished the heparhormone for experimental use, offering explanation of the product and suggestions for its use, for which we extend grateful thanks.



TABLE VII. EFFECT OF HEPARMONE ON LATE GESTATIONAL TOXEMIA  
(HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA)

Total cases Group A			2
<i>Average</i>	<i>Before</i>	<i>After</i>	
Blood Pressure	160/80-190/110	140/80-180/110	
Blood Urea Nitrogen	14 mg.	13.0 mg.	
Blood Uric Acid	5 mg.	3.5 mg.	
CO <sub>2</sub> vol. per cent			
Blood Sugar	81 mg.		
Van den Bergh	normal	normal	
Average quantity injected per case			80 c.c.
Number cases of eclampsia after heparmone			0
Total cases Group B			6
<i>Average</i>	<i>Before</i>	<i>After</i>	
Blood Pressure	148/94-222/118	138/88-220/110	
Blood Urea Nitrogen	12.0 mg.	12.0 mg.	
Blood Uric Acid	4.0 mg.	3.6 mg.	
CO <sub>2</sub> vol. per cent	56.0	51.0	
Blood Sugar	76.0 mg.	94.0 mg.	
Van den Bergh	normal	normal	
Average quantity injected per case			280 c.c.
Number cases of eclampsia after heparmone			1
Total cases of eclampsia in 3 years			23
Total cases of eclampsia in which heparmone was used			9
Results:			
Cases requiring additional treatment			8
Cases requiring operative interference			5
Deaths			0

TABLE VIII. USE OF HEPARMONE IN LATE GESTATIONAL TOXEMIA

<i>Type A. Toxemia</i>		Total	9
Average maximum blood pressure		188 mm.	
Average maximum reduction under heparmone		43 mm.	
Urinary improvement			3
Symptomatic improvement			6
Result:			
Labor induced			3
Baby died			1
Terminated in eclampsia			0
<i>Type B.</i>		Total	9
Average maximum blood pressure		200.0 mm.	
Average maximum reduction under heparmone		31.1 mm.	
Urinary improvement			1
Symptomatic improvement			2
Result:			
Labor induced			6
Baby died			5
Terminated in eclampsia			0
<i>Eclampsia</i>		Total	9
Average maximum blood pressure		173 mm.	
Average maximum reduction under heparmone		44 mm.	
Relief of convulsions			2
Operative interference			4
Result:			
Mother died (insufficient heparmone—1)			2
Baby died			5

TABLE IX. CYSTOSCOPIC STUDY OF "NORMAL" PREGNANCIES  
(LATE PREGNANCY)

Total	15
Hydronephrosis (moderate)	11
Multiparae      right 1      left 0      bilateral 1	
Primiparae      " 7      " 0      " 2	
Cultures:	
Reported "no growth"	5
B. Coli	3
Hem. Strep. pyogenes	1
Hem. Staph. albus	2
Diff. Indigocarmine (average)	
Right, 8 min., left 8 min.	
Evidence of ureteral edema	6

TABLE X. CYSTOSCOPIC DIAGNOSIS OF 119 CONSECUTIVE GYNECOLOGICAL  
PATIENTS FROM MAY 1, 1926, TO MAY 1, 1929

1. Cystitis		16
Acute	4	
Chronic	12	
2. Pyelitis		39
Right { Acute	0	
Chronic—coliform	15	
Other	10	(Including pus but no growth.)
Left { Acute	0	
Chronic—coliform	4	
Other	1	
Bilateral { Acute	4	
Chronic—coliform	4	
Other	1	
3. Hydronephrosis		14
Right	11	
Left	2	
Bilateral	1	
4. Pyonephrosis		
Right		1
5. Ureteral obstruction		14
Kink	1	
Calculus	3	
Stricture		
Right (Postoperative—3)	6	
Left	2	
Congenital narrowing—left	2	
6. Normal cystoscopy		
7. Questionable diagnosis		19
8. Tuberculosis		8
9. Nephroptosis		2
Right		
Bilateral		1
10. Urethral stricture		1
11. Vesicovaginal fistula		1
12. Horseshoe kidney		1
13. Urethritis		1
		119

(One-half of the total showed pyelitis or hydronephrosis without obstruction; of this number (53) 39 had borne children or miscarried, of whom 23 noticed the onset during pregnancy or shortly after.)

These trials were endorsed by our personal observation of the work of Miller and Martinez, whom we found earnestly endeavoring to follow their use of heparmone with individual attention and careful thought.

The opinions accompanying the above heparmone reports may be briefly expressed as follows:

Heparmone will reduce blood pressure, but for the most part only during treatment.

It must be supplemented with other measures.

It produced headache in many instances; instituted convulsions in one case; caused very sharp reaction in one case.

Very favorable improvement maintained after discontinuance of injections was noted in four women.

After the work of Duncan and Seng, Kretschmer, and others, we hesitate to include the "normal" table, which shows usual conditions. Of much interest, however, is the list of gynecologic urologic conditions.

Finally, from an attempt to combine the reference articles, and from the foregoing tables, certain conclusions appear sound:

1. Cystoscopic urologic diagnosis is an important part of an obstetric service, and when carefully performed carries no undue risk.

2. Vasodilatation and circulatory stasis of the distal ureter may directly or indirectly be concerned with late gestational toxemia.

3. Early and late toxemia are essentially different; the latter is primarily renal in origin.

4. Heparmone appears to bear insufficient specific action to separate a hepatic type from the late forms of pregnancy toxemias.

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When an ovarian cyst is discovered during the first trimester the accepted form of treatment is oophorectomy. However, Brouha feels that where the cyst is not discovered until the latter months, this procedure may result in either premature labor or rupture of the abdominal wall at term. In those cases where the cyst is in front of the presenting part an attempt should be made to displace it into the abdominal cavity by vaginal manipulation in either the knee-chest or Trendelenburg position. When such procedure fails, the patient should be allowed to labor until delivery from below could be accomplished if this cyst would not be interfering. At this time the abdomen is opened, the cyst removed and the pedicle ligated. The patient is then placed in the lithotomy position and delivered by either forceps or version. Following delivery the pedicle is reinspected for possible hemorrhage and the abdomen closed. Brouha advocates this procedure because he feels that closure is made easier after reduction in size of the abdomen and because occasionally the ligature on the pedicle may slip during delivery. Delivery from below is preferable to cesarean because the uterine wall is not subjected to surgical damage.

THEODORE W. ADAMS.

## THE SIGNIFICANCE OF LOW ARTERIAL PRESSURE IN PREGNANCY

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THE development of the sphygmomanometer gave such a marked stimulus to the study of the physics of the circulation that the use of this instrument has resulted in a magnitude of clinical observations on the cardiovascular mechanism. The application of blood pressure readings to the practice of obstetrics has become universal; particularly have we come to recognize the value of a rising blood pressure as a sign of impending toxemia. In recent years excellent studies have been made upon the course and effect of pregnancy in women with constantly raised blood pressures, the so-called essential hypertension.

In a notable manner low arterial pressure, hypopiesis, has received, in comparison with hypertension, scant attention by clinicians except in the past few years.<sup>1</sup> To my knowledge no discussion of this disturbance of the cardiovascular mechanism as regards pregnancy and labor has been offered, so that I have felt that a brief review of the subject, and an analysis of the histories of fifty women who presented marked hypotension, in one or more pregnancies, with a view to determine whether or not hypotension has any degree of significance as regards the course of pregnancy and labor, might be of considerable interest.

It would be difficult to define hypotension without some statement as to what constitutes normal pressure. Perhaps Faught's rule<sup>2</sup> is as accurate as any offered: "Begin at 120 mm. systolic for an adult male of twenty years and add one point for each two succeeding years. Women have a slightly lower pressure than men." Barach,<sup>3</sup> in discussing hypotension, states that for the sake of uniformity with others, he has adopted the level of 110 mm. of mercury, or less, as indicating arterial hypotension. Osborne<sup>4</sup> says that a systolic pressure of 110 mm. or lower in an adult should be considered hypotension, and even goes so far as to state that anything below 105 mm. calls for treatment, while a systolic pressure of 100 mm. or lower in an adult calls for rest from active duties. Norris<sup>5</sup> says when the pressure goes below 105 mm. few can be on their feet regularly.

In order to accentuate whatever significance low arterial pressure may have in pregnancy I have chosen for review in this paper only those women whose systolic pressures did not rise above 100 mm. during their pregnancies. This figure is considered by Janeway<sup>6</sup> as more truly indicating hypotension.

Cases presenting low arterial pressure are divided clinically into three groups without much difficulty. With acute hypotension we are all familiar. This includes the acute traumatic type, the case of surgical shock, the fall in pressure following prolonged anesthesia, the rapid fall in allergic reactions, and the acute drop often seen at the onset of epidemic influenza. In this group also belong those cases of temporary low blood pressures of the acute infections, influenza, typhoid fever, diphtheria, and pneumonia, and of the early weeks of pregnancy when even moderate hyperemesis gravidarum is present. A chronic low arterial pressure, the second group, is well recognized as a fairly constant finding in tuberculosis, the anemias, myocardial degenerations from such various causes as postinfluenzal weakness, focal infections, and various intestinal disorders including splanchnoptosis. Essential hypotension, the third group, is a condition of persistent low systolic pressure having no obvious exciting cause. For this condition we find many synonyms, the number and terminology of which may be indicative of the failure to properly explain its etiology: neurocardiovascular asthenia, hypoadrenia, hyposphyxie syndrome (Martinet), X-disease (MacKenzie), and constitutional hypotension (Riesman).

The frequency of the last group in general physical examinations, martial and civil, runs about  $3\frac{1}{2}$  per cent.<sup>2</sup> Larimore<sup>7</sup> feels that about 19 per cent of women have hypotension, and according to the physical type of the individual, using Mills's<sup>8</sup> classification of hypersthenic, sthenic, hyposthenic, and asthenic, considers that 64 per cent of the latter two classes have hypotension.

The production of normal blood pressure is dependent upon several factors: cardiac tone, the condition of the vessel walls, the peripheral resistance to the blood stream, and the state of the blood itself, volume and viscosity. Friedlander,<sup>9</sup> who has made an exhaustive study of the subject, considers peripheral resistance the most important single factor in the maintenance of normal pressure and the production of hypotension. The state of tonic contraction in which the arterioles and capillaries are normally held is due to impulses derived from vasomotor centers, subject to the rise and fall of these impulses as influenced by various stimuli. Capillaries possess a power of dilatation and contraction independently of the arterioles, and normally they maintain a state of vasomotor tone subject to both chemical and nervous stimuli. The potentially large reservoirs of the capillary bed may form an important factor in the low blood pressure of shock.

Mufson<sup>10</sup> has shown that in cardiovascular hypertensive toxemia the state of the capillary pressure is of prognostic value. A study of this phase of the vascular phenomena in pregnancy which I am making, especially in regard to hypotension, is of too recent beginning to offer any figures or deductions.

According to Friedlander the following theories have been offered to explain the low systolic pressure of essential hypotension: adrenal insufficiency (Lawrence); focal infection (Hoxie); respiratory deficit and decreased oxygenation (Barach); a constitutional inferior state (Levinson); elongation of the ascending aorta with narrowing of its semicircle (Fossier); a splanchnic pooling of the blood (Mosenthal), (Greaves); while Friedlander leans toward capillary stasis due to chronic poisoning from absorption of histamine or histamine-like bodies. Eyster<sup>11</sup> considers hypotension to be due to the dissemination of depressor substances which cause a dilatation of the peripheral vessels and a lowered capillary pressure, though the venous pressure remains the same.

Hypothyroidism and the clinically similar endocrine disturbances cause hypotension according to Barach from a decreased oxygenation consequent upon a lowered basal metabolism. Wright<sup>12</sup> points out that removal of almost the whole of the suprarenal gland has no effect upon the blood pressure of experimental animals. He dismisses the theory of hypoadrenia as a cause of low tension. Moody, Van Nuys and Chamberlain<sup>13</sup> found that 87 per cent of healthy athletic women students at the University of California had the greater curvature of the stomach below the interiliac crest. This finding, when one remembers that splanchnoptosis is given as a cause, shows that no sweeping conclusions should be drawn between constitution and body function. According to insurance companies there has been a very perceptible decrease in systolic pressure and a still more decided decrease in diastolic pressure within the past eight years, which may be partly accounted for by the increase in influenza.

The essential physical characteristics of a typical hypotensive adult picture a constitutionally underdeveloped inferior type; undersized, slender bodies, of a nonathletic build, with narrow nostrils and long necks they present drooping shoulders over a long narrow chest. They are shallow breathers with chest capacity smaller than normal, the costal angle is acute and the ribs consequently slant downward. The diaphragm is pushed downward and flattened, and the epigastrium is sunken above a protuberant hanging abdomen. Often the lumbar spine is straight, or even convex, rather than with a concave curvature.

Their chief complaints are physical exhaustion, lack of endurance and headaches. Such individuals become exhausted physically and mentally very quickly. Graham-Stewart<sup>14</sup> explains their capability of very considerable physical effort as being due to the overtone of the nervous as compared with the vascular system. Memory is often impaired. They complain of vertigo, fainting spells, and persistent headaches. From the circulatory system such symptoms as cold hands and feet or moist, clammy, numb extremities and cyanosis are complained of. While the skin and conjunctiva may present an anemic appearance often the hemoglobin and erythrocyte figures are normal. Many

of these symptoms are probably due to the deficient physical structure or to such associated conditions as splanchnoptosis, and not to the low pressure. Such marked symptoms as those pictured above are seldom seen with levels above 110 mm., but when they fall below this mark they will nearly always be followed by some subjective symptoms.

The prognosis as to life in cases of persistent low pressure is better than in cases where the pressure is normal or above. Fisher<sup>15</sup> of the North Western Life Insurance Company has stated that the death rate in the low pressure series was only 35 per cent of the expected mortality. As a rule these individuals do not lead as strenuous lives as those with higher pressures, and this inactivity may tend to longevity. There is a widely accepted impression that an individual with a decidedly lowered blood pressure is not a good surgical risk, based upon the idea that there is too narrow a margin between safety and shock. Frazer<sup>16</sup> urges that operation on a patient showing persistent low blood pressure should be delayed, if possible, until means have been taken to raise the blood pressure. In his requisites for an elective gynecologic section Polak<sup>17</sup> calls for a blood pressure between 110 and 150 mm. and states that blood pressure has a signal significance in the prognosis of operative patients. Graham-Stewart says that patients with hypotension are not bad operative risks, and that there is no great possibility of shock, possibly because the cardiovascular system is incapable of response.

#### CLINICAL DATA

*Age and Parity.*—In analyzing the histories of the 50 women who presented marked low arterial pressure during one or more pregnancies I found that their ages were mostly within the third decade. The 32 primiparous women had been married from three to ten years before pregnancy ensued. Nineteen of them stated that no contraceptives had been used, and in 5 of them various operative measures had been used to relieve sterility. It is possible that the same etiologic factor of the delayed pregnancies in these women may also be a cause in other sterile women who frequently present hypotension. Twenty-one children and 6 miscarriages had occurred among the multiparous women; for the social class of patient observed I feel this a larger than normal proportion of miscarriages, one premature infant died and there were two unexplained stillbirths before term. Fifteen of the 18 children had been bottle-fed from birth.

*Medical History.*—An effort was made by careful questioning to determine in the previous medical history some cause for the low blood pressure. There were 8 patients with a fairly definite history of ptosis of the stomach, including that of treatment in 3, and 1 of ptosis of the kidney. Influenza had attacked 10 of the patients during the epidemic of 1918, others gave a history of mild influenza in later years. Four



had been treated for cardiac disease, while 2 gave a history of rheumatic fever and 3 of diphtheria, both of which infections, as well as the influenza, may have left a weakened cardiac muscle. Three women gave a history of tuberculosis, 1 of the lung, 1 of the hip joint, and 1 of the glands of the neck. There were 2 others whose diseases of the bones, periostitis and curvature of the spine, pointed to tuberculosis. The menstrual histories showed a delay in onset until fifteen years in 12, and until seventeen years or later in 7 of these hypotensive subjects. Another related a history of epistaxis monthly from fourteen to seventeen years of age when the menstrual flow was normally established. In their previous pregnancies there had been severe enough nausea and vomiting to confine seven of the women to bed for at least two weeks. The symptoms of effort-exhaustion cropped out often in the histories of the multiparous women, and one had had a quite severe anemia. Among the 21 labors, forceps had been used 11 times, version once and bag induction had been done 2 times with prolonged but spontaneous deliveries.

*Nutrition and Weight.*—In regard to nutrition and weights, as compared with the medicoactuarial tables for age and height, 20 of the women were from 5 to 15 pounds below normal, 10 from 15 to 35 pounds underweight, 13 were within 5 pounds of the calculated normal, and 7 were well overweight. This frequent finding of hypotension in association with underweight is well recognized as a common occurrence in the examination of large groups of individuals. Concerning the constitution and physical characteristics of these women, when one attempts to classify them by Mills's classification, there were no hypersthenics, 22 sthenics, 2 hyposthenics and 26 asthenics. In other words there was an almost equal division of these women into sthenics and asthenics. The overweight women were held to an average gain in the last six months of  $11\frac{1}{2}$  pounds, those who were underweight, in spite of free feeding, could not be raised to an average of over 13 pounds, this included one woman who gained 54 pounds during her twin pregnancy.

*Blood Pressure.*—At least 8 estimations of the blood pressure were made on each of these patients. The initial pressure readings of all women in the group averaged 92 systolic and 58 diastolic. No pressure exceeded 100 mm., except for the 1 woman who developed eclampsia. The average low pressure readings were 82 and 56, the average high pressures during the period of observation were 94 and 64; in 6 of the women the maximum pressure never rose above 90 mm. The relation of the systolic pressure to the diastolic pressure and the pulse pressure remained in the ratio generally accepted for normal cases, 3 to 2 to 1, instead of the more frequent ratio of 5 to 3 to 2 in some series of recorded observations on nonpregnant hypotensive individuals.

*Physical Findings.*—Examination of the heart showed that, in addi-

tion to the 4 patients who had been treated for cardiac disease before pregnancy began, there were 6 with mitral systolic murmurs, 1 with an aortic systolic murmur, and in 19 it was noted that there was a poor heart tone. Treatment of these patients with digitalis and strychnin produced no effect upon the blood pressure. Strychnin produced a sense of stimulation in some of them, and in some instances a slight rise always followed a course of strychnin. Ephedrine was given without success to 2 women, while pituitary gland did not show any effect upon the systolic pressure. The basal metabolic rate in 6 patients who apparently had hypothyroidism was within the normal limits, minus 10 to plus 5. In these and in several other similar instances thyroid gland was exhibited without any change in the pressure. In about half of the series, it appears from a graphic chart, there was a moderate rise in the systolic pressure at about seven and one-half months, this rise was not sustained, however, and may indicate that this time represented the acme of metabolic activity on the part of these women.

*Symptomatology.*—Anemia, of the so-called physiologic type of pregnancy, was frequently noted. Six women showed a hemoglobin of 75 per cent, and 13 a reading of below 75 per cent, with a reduction of the red cells to below 3,500,000. In none of the women was the pernicious type of anemia of pregnancy seen. There was administered to those with anemia various combinations of iron and arsenic by mouth or by hypodermic with variable results. The average low systolic pressure was 80 mm. In so far as the effect of this therapy upon the pressure was concerned there was an average rise of 10 points systolic and 12 points diastolic following treatment. So it may be assumed that intensive treatment of pregnancy anemias reflexly influences the cardiovascular mechanism. In no instance were positive Wassermann reactions obtained.

Dyspnea and fatigue were most frequent among the subjective symptoms; effort-exhaustion, headaches, sleepiness, and mental dullness were complained of by over half the patients. Attacks of mental depression and "nervous spells" were prominent subjective phenomena.

Toxemia appears relatively infrequently among these women, but 1 patient developed eclampsia, postpartum, after a rising blood pressure in late pregnancy, with albuminuria, for which a bag induction was done. This patient with an initial blood pressure at the second month of 90-60, had 100-60 at the thirty-sixth week. Two weeks later there was marked edema, albuminuria and the systolic pressure had risen to 120 mm., she had gained 54 pounds during the pregnancy in spite of remonstrances against her gross appetite, and as evidence of kidney involvement became more marked as induction was done. The labor was long and slow, twins were delivered by low forceps and version. Several convulsions developed during the first six hours after delivery with the blood pressure rising to 174-96 at one time.

The patient recovered, and the pressure quickly fell to its former low level where it has remained over a period of five years. Eight of the patients of the series developed definite albuminuria and edema of the ankles in late pregnancy without any rise in pressure. It appears that in at least one instance the definite rise from a hypotensive level was just as suggestive and prognostic of impending toxemia as a similar rise in a normal pressure individual, and such rise should not be regarded with equanimity. Several times when a reading was made immediately postpartum there was never a drop in the systolic pressure of over 10 points. The lowest systolic pressure recorded was 60 mm. with no evidence of shock.

*Obstetric History.*—Any constitutional inferiority as a causative factor in the production of the low systolic pressure was not reflected in a marked degree of pelvic infantilism as a stigma. In accordance with what one might expect from their physical configuration and stature 11 of the women showed just minor pelvises. Two had generally contracted pelvises, one a flat pelvis, and 2 had narrowing of the transverse diameter of the outlet. Five infants were delivered with low forceps, 6 with midforceps, cesarean section was done twice for contracted pelvis, and version once upon a twin. Breech extractions were done 3 times. The duration of labor showed an average of twelve hours for the multiparous women, thirty-one hours for the primiparous women and twenty-one hours for all labors in spite of the number of premature and forceps deliveries; in all a rather definite prolongation of the duration of labor as contrasted with normal labors.

The average weight of the babies born to primiparas was 6 pounds and 1 ounce, to the multiparas, 7 pounds and 4 ounces. Nine babies were born prematurely from four to eight weeks, 4 of them died; in addition one subnormal baby with both arms absent died during the first week, and an anencephalic monster died immediately after birth. Of the premature babies 2 weighed under 4 pounds and 4 under 5 pounds. It will thus be seen that in this series there was a tendency to lowered weight of the primiparas' babies, and a marked increase in the usual ratio of premature deliveries. Whether this is significant, or not, is speculative; it can hardly be proved that these results depended upon the finding of a low blood pressure in the mothers, but at least the results point to the mothers being substandard. The ability of these women to nurse their babies was quite poor, but 15 were nursing their offspring in whole or in part when they left the hospitals.

*Follow-Up.*—The follow-up on these women at their final examinations from four to twelve weeks after delivery, to several years later, showed an average blood pressure of 94 systolic, 66 diastolic, there had been a sustained rise in none of them. The average weight loss from the recorded maximum recorded, on the occasion of the final examination, was 17 pounds.

## DISCUSSION

Hypotension, systolic pressure of 100 mm. or less, occurs among about 5 per cent of pregnant women in early adult life. Many of these patients showed a late development of sexual maturity as evidenced by delayed appearance of the menstrual flow. Hypotensive women do not seem to be quickly fertile after marriage, and it is possible that this etiologic cause of delayed pregnancy may also be a factor among other sterile women who frequently present a hypotension.

One-fifth of the number of patients studied had had severe attacks of influenza within recent years. Other infectious diseases had occurred in about the usual frequency. Definite cardiac disease or weakness, and presumable myocardial insufficiency, was present in nearly half the patients. Tuberculosis was definitely present in 1, suggestively in 4. Degrees of ptosis of the abdominal organs were found in one-sixth of the women, some of whom had had symptoms sufficient to warrant treatment.

Of the women who were first seen after passing through one or more pregnancies, there was a history of one-fourth having had marked nausea and vomiting. The ratio of miscarriages was well above normal. The symptom-complex, fatigue-exhaustion was often noted, the labors had been long and ended by an unusually high number of operative deliveries.

Underweight was noted in 60 per cent of the patients studied, which finding corresponds to other correlated studies of weight and blood pressure. An attempt to classify this series of patients according to their physical characteristics resulted in dividing them into two groups, the sthenic and the asthenic, with a slight preponderance of the latter. When this grouping was compared with the nutrition analysis most of the underweight women fell into the asthenic group. There was an almost total absence in this series of that type of woman described by Draper<sup>18</sup> as being subject to the cardiovascular hypertensive type of toxemia of pregnancy. The difficulty of building up these undernourished and asthenic individuals may be seen from the fact that an average of but 13 pounds, including 1 gain of 54 pounds, could be added during the last 2 trimesters in face of what in some examples amounted to forced feeding.

The blood pressure readings showed a definite hypotension, and the average readings ranged from a low of 82 over 56 to a high of 94 over 64. In about half the cases a graphic chart showed a rise up to about the thirty-fifth week, which may have represented the acme of metabolic activity on the part of these women. The ratio of systolic, diastolic and pulse pressure remained in a normal ratio, 3 to 2 to 1. Treatment of cardiac conditions, or of the apparently weak myocardial muscle, by strychnin or digitalis did not have any sustained effect upon the systolic pressure. Other drugs, as ephedrine, thyroid and

pituitary, seemed of no effect. Treatment of the anemia, of the so-called physiologic type, in 26 per cent of the patients showed an apparent sluggishness on the part of the hematopoietic system. There was but a slight bettering of the anemia and a moderate rise in the pressure consequent upon the treatment.

These women complained in a degree quite above normal of physical inability, dyspnea and headaches while vertigo, mental dullness and psychic depression were frequently recurring subjective symptoms.

Aside from a few mild albuminurias with no coincident rise of pressure but one case of definite toxemia developed. This was no doubt a metabolic upset consequent upon an enormous gain in weight, eclampsia developing postpartum, after an induced twin labor, with recovery, and an early return, with persistence, to the former low systolic pressure. A rising systolic pressure is undoubtedly as significant of impending toxemia here as in a case with normal pressure. These women are almost wholly the very antithesis of the type developing the hypertensive form of toxemia of pregnancy.

The duration of labor showed quite an increase in the time usually required for normal spontaneous deliveries. In multiparas the average was twelve hours, in primiparas thirty-one hours, for all labors, including operative deliveries, twenty-one hours. Forceps were used 11 times, section was done twice, and version once, upon a second twin. The delay in the labors from a study of the histories was apparently equal for the two stages, and may be taken as an indication of the inability of the hypotensive type of woman to normally complete her physiologic task. There was an equally marked reflection of this inability in the larger proportion than usual of premature babies, 9 being born from four to eight weeks prematurely. The average weight of the baby born to the primiparous woman, 6 pounds and 1 ounce, may again reflect upon an originally poor germ plasma, as might also the two abnormal infants, one an anencephalus. The primiparous woman was as little able to nurse her infant as the multiparous, but 15 women were nursing their babies, in whole or in part, at the end of two weeks.

Estimation of the blood pressure and weight weeks or months after delivery showed that the stimulus of the metabolic activities of pregnancy had had no effect upon nutrition or the cardiovascular mechanism, the blood pressures persisting at their former low levels. There did not seem to have been any more marked tendency to errors of involution or to displacements than in the normal woman.

#### SUMMARY

Definite hypotension occurs in 5 per cent of pregnant women. These women often mature late and are relatively infertile. A certain proportion of them have had influenza, have weak cardiac musculature or

have an anemia. They are often of an asthenic build, as frequently underweight, and are difficult to build up. Treatment by various measures uniformly fails to raise the blood pressure appreciably. Their pregnancies are characterized by a high percentage of miscarriages and premature labors. Their children are smaller than normal. They complain greatly of effort-exhaustion, dyspnea, headaches and nervous depression. Tendency to toxemia is relatively slight. They suffer from prolonged labors, characterized by inertia, and operative interference is much more frequent than in normal women. They are largely unable to nurse their babies. The stimulus of pregnancy has no effect later on of raising the blood pressure.

Low arterial pressure in such patients may be but an expression of a constitutionally inferior, physically and in a reproductive sense, type of woman, and is often significant of her obstetric unfitness.

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# BASAL METABOLISM STUDIES IN NORMAL PREGNANT WOMEN WITH NORMAL AND PATHOLOGIC THYROID GLANDS

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IT IS generally agreed that there is a definite increase in the basal metabolic rate during the latter part of normal pregnancy, but that this increase is "due to the increasing mass of active protoplasmic tissue, consisting of a large part of the fetal tissues and in lesser part of maternal structures" (Sandiford and Wheeler<sup>1</sup>), and is very moderate in extent. This argument is supported by the fact that subtraction of the calculated heat production of the fetus from the total heat production of the pregnant woman leaves the metabolic rate of the latter unaffected by gestation, and by the observation that almost immediately after delivery the metabolic rate falls to a point corresponding with that obtaining in early gestation or before conception.

When expressed in terms of the Aub-Dubois prediction standards, the total increase due to the rapid metabolism in the fetal tissues rarely amounts to more than 15 per cent. If one accepts the statement of Benedict<sup>2</sup> that all prediction standards are 5 per cent too high for normal women, the normal metabolic rate would range from minus 15 to plus 5 per cent according to the standards now in use. Using an increase of 15 per cent during pregnancy as the maximum which may be attributed to an augmentation of the active protoplasmic mass, it would be reasonable to view as potentially abnormal any rate above plus 20 per cent. However, Gustafson and Benedict<sup>3</sup> insist that even among 10 presumably healthy individuals at least one or more "will have a metabolism deviating more than plus-minus 10 per cent from the standards." This would lead one to anticipate readings of slightly higher or lower values in 10 to 20 per cent of any series. Mussey, Plummer, and Boothby<sup>4</sup> say that "a basal metabolic rate of plus 25 or even plus 30 is not necessarily an indication of hyperthyroidism in the latter months of pregnancy," and thus recognize the occasional variations pointed out by Gustafson and Benedict.<sup>3</sup> It would seem to be well demonstrated that a high basal metabolic rate unsupported by clinical evidence of hyperthyroidism does not warrant a diagnosis of abnormal thyroid activity.

In order to add further confirmation to the various previous reports on the basal metabolism of normal pregnant women with normal thyroid glands, and to investigate the metabolism in various varieties of

thyroid hypertrophy, we have studied 72 women through gestation and for several weeks after delivery. Our patients divide themselves into four groups, according to the clinical condition of the thyroid gland.

Normal thyroid gland	21 cases
Small colloid (endemic) goiter	23 cases
Adenomatous goiter	18 cases
Large colloid (visible) goiter	10 cases

Clinical differentiation of patients was made at their first visit to the clinic, upon the basis of careful palpation. Additional clinical observations were made at monthly intervals during pregnancy, and more frequently in the puerperium. All metabolism tests were made by the regular laboratory technicians as a part of their routine work. Aub-Dubois standards were employed and the technic outlined by Boothby and Sandiford<sup>5</sup> was followed in detail, the patients coming to the laboratory between eight and nine o'clock in the morning, the last food having been taken the preceding evening. Tests were made at four-week intervals, usually from the fourth lunar month. After delivery, two or three determinations were obtained during the first two weeks and another, if possible, at six weeks. The results of tests which were for any reason unsatisfactory were discarded, accounting for various breaks in the series. Private patients alone were utilized and full cooperation was demanded. A predominance of primiparous women is explained by the fact that it is generally easier for them to keep early morning appointments.

#### NORMAL PREGNANCY: NORMAL BASAL METABOLIC RATE

Compilation of the results showed that in each group there were numerous patients who had unquestionably normal metabolic rates which never rose above plus 20 per cent. Such determinations upon 48 individuals have been combined in a single chart (Fig. 1) with the median shown by the heavy dotted line. The average increase in the basal metabolic rate is from plus 1 per cent in the third to plus 9 per cent in the tenth lunar month, while during the first week after delivery the rate falls to plus 1, the early pregnancy point. In the later puerperium, there is a progressive slight fall to an average of minus 7 per cent during the third week. This curve is consistent with the results of previous workers (Sandiford and Wheeler,<sup>1</sup> Rowe, Alcott and Mortimer,<sup>6</sup> Root and Root,<sup>7</sup> etc.), and confirms the observation that lactation is not associated with an increased metabolism. Diminished physical activity has been held largely responsible for this observed postpartum fall in the basal metabolic rate.

Utilizing other data obtained when the metabolism tests were made, it was possible to construct the curves for average variations in weight, pulse, and blood pressure, as well as for the metabolic rate. The general similarity of the curves as plotted is striking. The weight



shows an average gain during pregnancy of 17 kg. (37½ pounds), with a loss at delivery of 9 kg. (20 pounds), and an apparent permanent gain to the body of 8 kg. (17½ pounds). There is a slight increase in the pulse rate as pregnancy advances, with a drop to normal shortly after delivery. The blood pressure tends to be low early in gestation, but undergoes a rise in the last month, and a slow fall during the puerperium.

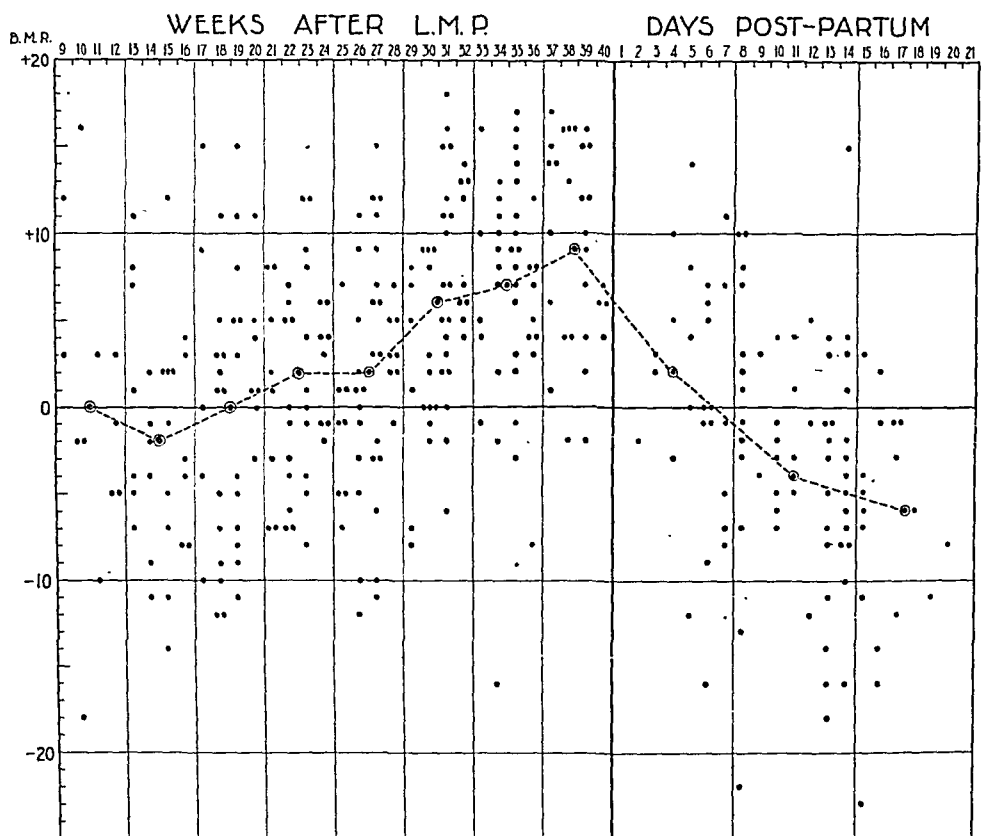


Fig. 1.—Basal metabolic determinations among 48 normal pregnant women with normal thyroid activity. Each dot represents a single satisfactory reading.

Twenty-two of the patients in this group were given sodium iodide (4 grains per day for ten days) at intervals of two or three months throughout the pregnancy, 9 patients used iodine salt exclusively during gestation, and 17 had no iodine added to the diet. It cannot be shown that the use of iodine was reflected in the metabolic rate. Examinations of the thyroid glands of the newborn babies, however, revealed that among the 17 women who had no prophylactic iodine, 5 gave birth to babies with appreciably enlarged thyroids, whereas congenital goiter was not noted in any instance where the mother took iodine.

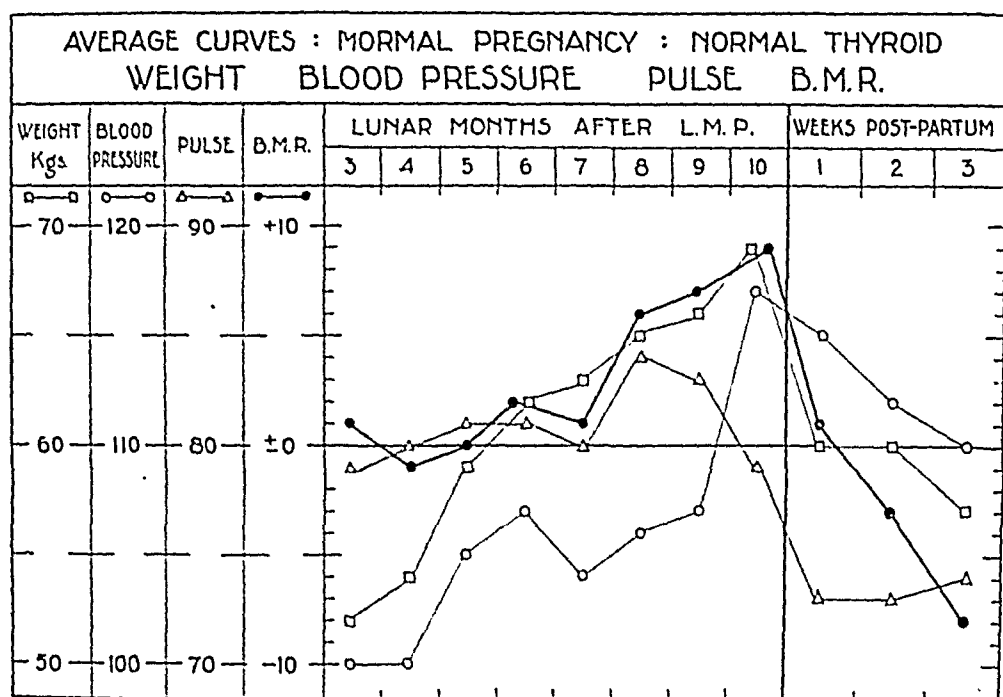


Fig. 2.—Average pregnancy changes in pulse, blood pressure, weight, and metabolic rate as deduced from data on 48 normal pregnant women.

#### NORMAL PREGNANCY: INCREASED BASAL METABOLIC RATE

Twenty-four (33 per cent) of the 72 patients studied showed metabolic rates above the chosen standard of plus 20 per cent on one or more tests, and were subjected to closer study. The distribution of these cases among the various clinical groups was as follows:

THYROID GLAND	NORMAL B. M. R.	B. M. R. ABOVE PLUS 20	TOTAL
Normal	16	5 (24%)	21
Small colloid goiter	15	8 (35%)	23
Adenomatous goiter	12	6 (33%)	18
Large colloid goiter	5	5 (50%)	10

Palpable evidence of thyroid hypertrophy is apparently associated with a greater tendency toward increased metabolism, as might well be expected. Our work does not, however, support the inference to be drawn from the report of Davis,<sup>8</sup> that all normal pregnant women who have thyroid hypertrophy show metabolic rates above normal.

The patients with increased metabolic rates (above plus 20 per cent) will be discussed separately according to the type of gland hypertrophy present.

#### NORMAL THYROID GLAND: INCREASED BASAL METABOLIC RATE

Five of 21 patients with normal thyroids had rates above plus 20 per cent, an incidence which is hardly above the average expectancy of increased metabolism. The great preponderance of plus readings should, however, be noted, with the tendency toward early pregnancy

values well above the average. On the other hand, it will be seen that after delivery the values are comparable with those of early pregnancy, with a decided second-week drop, which does not go below the zero line. The average increase during pregnancy is 15 per cent and the average first-week postpartum drop is 12 per cent. These curves follow the usual course but in each case the metabolism is constantly slightly above the average. Two of the patients, Cases 17 and 18, showed a definite pregnancy enlargement of the thyroid gland; two others, Cases 19 and 21, complained of increasing nervousness and presented tremors, while only one (Case 20) had no clinical evidence of thyroid change. In no case were the symptoms sufficiently marked to demand treatment, but it would seem that such individuals must be in a state of potential hyperthyroidism as a result of the pregnancy increase of metabolism.

NORMAL THYROID : NORMAL PREGNANCY : INCREASED B. M. R.																		
CASE NO.	AGE	PARITY	IODINE	WEEKS OF PREGNANCY								WEEKS AFTER DELIVERY						HYPER-THYROIDISM.
				3	4	5	6	7	8	9	10	1	2	3	4	5	6	
17	21	I	NaI 20, 26		+15		+5	+12	+15	+27	+25		+6					0
18	28	I	NaI 16, 24, 32	+4	+5	+10		+17	+2	+21		+12	-5					0
19	31	I	1.5.		+15	+20	+14	+18	+22	+29		+13	+5				±0	0
20	27	I	1.5.			+4	+10	-5	+12	+16	+24			+8				0
21	34	II	0						+24	+33	+30	+18	+14				+2	+

Fig. 3.—Basal metabolic rates in 5 normal pregnant women with normal-sized thyroid glands but with increased metabolism.

CASES 17 and 18, when examined two weeks postpartum, had symmetrical enlargements of the gland, which had not been noted previously, but signs of hyperthyroidism could not be elicited. Both infant thyroids were normal, due probably to the protection afforded by the sodium iodide administered during pregnancy. We feel that in these instances the thyroid enlargements were gestational phenomena.

CASES 19 and 20 showed no enlargement of the thyroid at any time. Iodine salt was used throughout the pregnancies. The infant thyroids were not enlarged. Patient No. 19 was unusually nervous and might be designated a hyperthyroid type, although clinical evidence of hyperthyroidism was not present.

CASE 20 had symptoms somewhat suggestive of very early exophthalmic goiter with characteristic eye signs and general nervousness, although the pulse rate was normal and no enlargement of the thyroid could be determined. No iodine was given during pregnancy. The infant had a congenital goiter, which led us to believe that the maternal thyroid function was abnormal and that the elevated metabolism was probably due to mild hyperthyroidism. Further study and a metabolism test one year after delivery failed to make a positive diagnosis, although the symptoms had persisted.

#### SMALL COLLOID (ENDEMIC) GOITER: INCREASED BASAL METABOLIC RATE

For the purpose of this study, an endemic colloid goiter is defined as a thyroid gland whose isthmus is distinctly enlarged but estimated to be not more than 2.0 cm. thick, and whose lobes show a palpable, sym-

metrical enlargement. In making such a diagnosis, the possibility of pregnancy hypertrophy had to be considered, but since the initial examination was usually made before the sixteenth week of pregnancy, when gestational hypertrophy is making its appearance, it is felt that these are instances of true endemic enlargement. The fact that our observations were carried out in a region of endemic goiter supports that view. Among the 23 patients in this group, there were 8 who showed metabolic readings above normal. (Fig. 4.)

In the majority of these patients, the metabolic readings in early pregnancy were above normal, and only Case 43 had a normal postpartum metabolism. In this case there was a twin pregnancy and in all probability the increased bulk of fetal protoplasm was responsible for the unusual rise in the metabolic rate. Cases 40 and 41 showed par-

SMALL COLLOID GOITER : NORMAL PREGNANCY : INCREASED B.M.R.																		
CASE NO.	AGE	PARITY	IODINE	WEEKS OF PREGNANCY								WEEKS AFTER DELIVERY						HYPER-THYROIDISM.
				3	4	5	6	7	8	9	10	1	2	3	4	5	6	
37	23	I	NoI 20.36					+3	+21	+24	+9	+7	+5	+3				0
38	25	II	NoI 16.24	+10	+3	-1	+18	+10		+21		+12	+15				+4	+
39	30	I	NoI 20.32			+4		+6	+22	+32	+37		+27	+13			-2	+
40	31	I	NoI 13.21,34	+24		+11	+11	+12	+7	+25			+7					0
41	21	I	NoI 20		+27	+17	+9	+14		+28	+5	+14	+10					0
42	28	I	NoI 20.28		+5	+9	+9	+32		+25		+15	+8					±
43	30	I	I.S.			-3	+12		+20	+16	+24		+2	-2				0
44	25	II	0		-2	+4		+7	+14	+24	+7	+12	+7					0

Fig. 4.—Basal metabolic rates in 8 normal pregnant women with endemic goiters and with increased metabolism.

ticularly high metabolism in the early months and relatively little increase as gestation progressed, with postpartum values below those in early pregnancy. Both patients received prophylactic iodine, which may have served to protect them from developing a much more rapid metabolism in the latter part of pregnancy, although our general experience would hardly warrant such an hypothesis. On the other hand, Cases 39 and 44 showed pregnancy increases of metabolism of 33 and 26 per cent, respectively, and following delivery had metabolic readings well above their early pregnancy values. It would seem that gestation had served to stimulate thyroid activity to some extent without leading to clean-cut symptoms and signs of hyperthyroidism.

These 7 cases, excluding No. 43, all gave positive or quite suggestive evidence of increased thyroid activity during pregnancy. The fact that they showed a return of the metabolic rate to normal during the puerperium, even though it was markedly delayed, leads us to feel

that the increased thyroid activity may well have been due to a stimulation of thyroid function brought about by the pregnancy.

CASE 37.—There was no increase in the size of the thyroid and no definite clinical evidence of hyperthyroidism was noted during the period of observation. The infant thyroid was normal in size.

CASE 38.—No increase in the size of the thyroid was noted during pregnancy. The infant thyroid was normal in size. Clinically, there were symptoms of a mild hyperthyroidism, fine tremor, tachycardia, and nervous manifestations.

CASE 39.—The thyroid showed a slight increase in size in late pregnancy which persisted into the puerperium. Clinical evidence of mild hyperthyroidism was present in the latter months of gestation and was especially noticeable after delivery. The infant thyroid was normal.

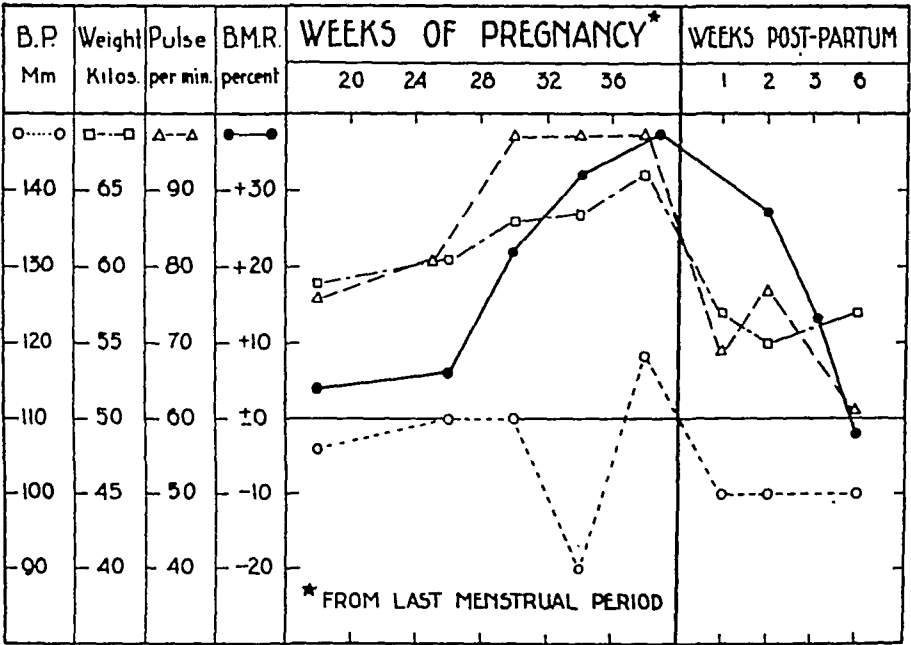


Fig. 5.—Case 39. Small colloid goiter showing definite, temporary thyroid hyperthyroid activity during pregnancy.

CASE 40.—This patient was of a neurasthenic type and was underweight at the beginning of pregnancy. During gestation there was a considerable gain in weight and a marked improvement in general health. There was a history of a slight hyperthyroidism, which had been treated medically some years previously. The thyroid did not increase in size appreciably during pregnancy, and no evidence of hyperthyroidism could be found. The infant thyroid was normal.

CASE 41.—Enlargement of the thyroid gland was first noticed at puberty, when a short course of iodine treatment was given. During pregnancy the gland did not increase in size, and there were no positive clinical signs of hyperthyroidism. The infant thyroid was normal.

CASE 42.—There was no previous history of goiter, and no increase in size of the gland was noted during pregnancy. Clinical evidence of hyperthyroidism was

lacking, except that the patient had a slight tachycardia, which persisted through pregnancy and the puerperium. The infant thyroid was normal.

CASE 43.—Twin pregnancy. Some thyroid enlargement was first noticed at the time of puberty, but was not treated. During gestation there was no apparent enlargement of the gland and there were no clinical signs of hyperthyroidism. The increased metabolism is probably explained by the multiple pregnancy. After delivery the curve fell rapidly to normal. The infant thyroids were not enlarged.

CASE 44.—The goiter probably dates from puberty. There was no enlargement of the gland during this pregnancy nor during the first gestation two years previously. No signs of hyperthyroidism. The infant thyroid was normal.

#### ADENOMATOUS GOITER: INCREASED BASAL METABOLIC RATE

All patients who showed palpable adenomas of the thyroid are grouped in this section. Since the determination was entirely clinical, it is possible that other small adenomas were missed and the patients placed in other groups. Of the 18 patients who had definite adenomas,

ADENOMATOUS GOITER : NORMAL PREGNANCY : INCREASED B.M.R.																		
CASE NO.	AGE	PARITY	IODINE	WEEKS OF PREGNANCY								WEEKS AFTER DELIVERY						HYPER-THYROIDISM.
				3	4	5	6	7	8	9	10	1	2	3	4	5	6	
57	31	I	0	+10	+4	+10	+11	+15	+19	+22	+25	+4	-1				-2	0
58	27	II	NaI 14, 28		+2	+10	+17	+25			+30	+26	+19	+18			+10	+
59	31	III	NaI 18, 24			+10	+15	+15	+25	+35		+21	+2				-6	+
60	41	II	NaI 10	+32	+41	+50	+29	-1	-5			-14		-11			-29	+++
61	28	I	0		+10	+5	+10	+8	+13	+28	+17	+14	±0				-2	++
62	37	I	0	+8	+15		+6	+27		+18	+34	+14	+15				+4	+

Fig. 6.—Basal metabolic rates in 6 normal pregnant women with adenomatous goiters and with increased metabolism.

6 had metabolic rates above plus 20 per cent together with clinical evidence of hyperthyroidism, except one case, and will be considered separately.

In general the rise in the metabolic rate during pregnancy is greater than in normal individuals and the postpartum drop is slower and less complete. Only one patient (No. 62) showed a definite increase in size of the gland during gestation. Three patients had prophylactic iodine and 3 were not treated. Among those who received sodium iodide, there was no evidence of congenital goiter in the newborn even though the thyroid enlargement was greater and the basal metabolic rate higher than in the other 3 who were given no iodine, and among whom there were two instances of congenital goiter in the infants. Only in Case 60 was there any reason to believe that iodine might have done harm and here the metabolic rate was considerably elevated (plus 32 per cent) before sodium iodide was administered, about the tenth week, when clinical symptoms of hyperthyroidism were already gradually increasing.

CASE 57.—No history of the time of appearance of the goiter could be obtained; there had been no previous treatment. There were no definite clinical signs of hyperthyroidism, and no increase in the size of the thyroid or of the adenoma was detected during pregnancy. The patient received no iodine therapy; the child showed a small congenital goiter.

CASE 58.—The goiter was first noticed at the time of puberty and some iodine therapy was employed at that time. At the third month of pregnancy, there was a visible goiter with adenomas in each lobe and clinical signs of a mild hyperthyroidism. Following sodium iodide (4 grains q.d. for ten days) in the fourth month of pregnancy, there was a slight decrease in size of the glands, with no further increase during the latter months of pregnancy. The metabolic rate was still above normal (plus 10 per cent) six weeks after delivery. The infant thyroid was normal.

CASE 59.—The goiter had been present for several years, enlarging during each pregnancy, but no definite history of its first appearance could be obtained. One year before the onset of this pregnancy medical treatment had been given and operation advised but refused. At the fourth month of gestation there was a visible goiter with multiple adenomas, and evidence of a slight hyperthyroidism with fine tremor, tachycardia, and nervous irritability. Sodium iodide was given during the fifth and the seventh lunar months and was followed by improvement of the symptoms. There was no change in the size of the gland during pregnancy. The infant thyroid was normal.

CASE 60.—The history of the appearance of the goiter is uncertain but the enlargement had been noted for some years, although the story did not suggest hyperthyroid symptoms. The patient was admitted to the hospital when nine weeks pregnant because of nausea, which was treated successfully by the usual suggestive therapy. When the vomiting ceased, a course of sodium iodide was given. During the next two months the symptoms of hyperthyroidism increased steadily and at the nineteenth week the patient was again hospitalized. Three weeks of bed rest together with the administration of Lugol's solution daily effected no improvement (very possibly the iodine was harmful) and finally at the twenty-second week a subtotal thyroidectomy was performed. After a stormy, early post-operative course, convalescence proceeded normally and the pregnancy continued uneventfully to term. After delivery a mild myxedema appeared and was treated with thyroid extract. The infant thyroid was normal.

CASE 61.—There was no history of onset of the goiter; no previous iodine treatment had been given. The thyroid increased definitely in size during pregnancy, and in the latter months there developed signs of hyperthyroidism (tremor and nervous manifestations), which persisted into the puerperium. The infant thyroid was moderately enlarged. This case seems to illustrate quite well the possible effect of pregnancy upon a thyroid gland which is not quite normal when gestation begins. Iodine therapy might have prevented the development of symptoms.

CASE 62.—The onset of the goiter was not noted; there had been no previous iodine treatment. Examination at the second month of pregnancy showed a palpable enlargement of the thyroid with a small adenoma in one lobe. No iodine treatment was given during pregnancy. The gland showed a definite enlargement during gestation. Late in pregnancy and during the puerperium there developed clinical signs of hyperthyroidism in the form of a fine tremor and various nervous manifestations. The infant showed a congenitally enlarged thyroid. After delivery, the metabolism remained elevated with a slow return to normal. The patient illustrates the train of signs and symptoms which pregnancy may produce in the presence of a goiter.

## LARGE COLLOID GOITER: INCREASED BASAL METABOLIC RATE

One-half of the large colloid goiter group developed elevated metabolic rates together with signs of hyperthyroidism, while the other 50 per cent pursued a course unaffected by gestation. The elevation of metabolism in the first 5 cases can, in all probability, be attributed to hyperactivity of the thyroid. Two of these patients had no prophylactic iodine during pregnancy and both infants were born with congenital goiters. Assuming that the rate of metabolism postpartum is an index of the activity of the thyroid, these patients all suffered from a mild hyperthyroidism. Colloid goiters frequently have little active thyroid tissue and the increased demands of pregnancy may well be expected to lead to an abnormal activity with resultant evidence of thyroid intoxication.

CASE 68.—The goiter was first noticed at the time of puberty and some iodine was given at that time. At the fourth month of pregnancy there was a visible enlargement of the thyroid and clinical symptoms of a mild hyperthyroidism. The

LARGE COLLOID GOITER : NORMAL PREGNANCY : INCREASED B.M.R.																		
CASE NO.	AGE	PARITY	IODINE	WEEKS OF PREGNANCY								WEEKS AFTER DELIVERY						HYPER-THYROIDISM.
				3	4	5	6	7	8	9	10	1	2	3	4	5	6	
68	29	I	NaI 17, 28			+14	+3	+15	+10	+23	+30		+5				+3	+
69	32	V	NaI 32						+19			+24					+12	0
70	30	III	NaI 19, 25	+23	+17	+30		+45	+31	+53	+50	+20	+23				+5	+
71	33	I	I.S.			+9		+23		+29		+23	+9				+31	±
72	24	I	0		-1	+7	+20	+29	+25	+44				+2				±

FIG. 7.—Basal metabolic rates in 5 normal pregnant women with large colloid goiters and with increased metabolism.

first course of sodium iodide at the fifth month was followed by a slight decrease in the size of the gland, with no further change apparent during the remainder of pregnancy. The infant thyroid was unaffected.

CASE 69.—The goiter was first noticed during puberty, and the patient received some iodine treatment at that time, but none later. An operation, probably ligation of the vessels, was done on the thyroid seven years previously. At the eighth lunar month of pregnancy, when first seen, there was a large symmetrical colloid goiter, which filled the front of the neck and gave slight evidence of pressure upon the trachea. There was no definite clinical evidence of hyperthyroidism. Sodium iodide was given during the ninth lunar month but did not protect the fetal thyroid which was somewhat enlarged at birth.

CASE 70.—The goiter dated from puberty when some iodine treatment was given. Examinations at the third lunar month showed a large, lobular, colloid goiter (Fig. 2), with evidence of mild hyperthyroidism. Sodium iodide given during the fourth and sixth lunar months did not affect the size of the gland, but did protect the fetal thyroid which was normal at birth.

CASE 71.—Onset of the goiter at puberty; no previous iodine treatment. Examination at the fifth lunar month of gestation showed an easily visible symmetrical



enlargement of the thyroid but no evidence of even mild hyperthyroidism. Sodium iodide given at the sixth month was followed by a definite decrease in the size of the gland, which showed no further change during pregnancy. The infant thyroid was normal.

CASE 72.—The patient does not know when the goiter first appeared; there had been no previous iodine treatment. Examination at the third month of pregnancy showed visible enlargement of the thyroid gland with no evidence of hyperthyroidism. Iodine was not administered during gestation and the goiter exhibited a palpable increase in size as pregnancy advanced. The infant thyroid was congenitally enlarged.



Fig. 8.—Case 69. Large colloid goiter.



Fig. 9.—Case 70. Large colloid goiter.

#### DISCUSSION

These studies would seem to indicate that pregnancy tends to place upon the thyroid gland an extra burden, which the perfectly normal gland is able to assume without great difficulty, but which causes certain disturbances in those individuals whose thyroids are already somewhat affected when gestation begins. The greater the original pathologic alteration in the gland, the greater the chance that pregnancy will lead to true hyperthyroidism. The determination of hyperthyroidism is a clinical problem but basal metabolic estimations are useful diagnostic adjuncts when interpreted correctly. An unusual increase in the metabolic rate during pregnancy, together with an early post-delivery reading above the early-pregnancy value and a slow return of the metabolism to normal, can best be interpreted as indicating a true pregnancy hyperplasia of the thyroid. Our conclusions in this regard agree with those reached by Davis.<sup>7</sup>

The use of prophylactic doses of iodine during pregnancy apparently has but little effect in preventing gestational hypertrophy of the thyroid (Cases 17 and 18), provided the gland is of normal size originally, but it is useful in preventing such an hypertrophy in colloid goiters and may even lead to a decrease in their size. (Cases 68 and 71.) The first of these statements is in contradiction to Davis,<sup>7</sup> who believes that "if a woman with a normal thyroid takes sufficient iodine during the course of a normal pregnancy, her basal metabolic rate will remain within normal limits, although it may show a gradual increase during the last weeks of pregnancy." Our different results may be due to the fact that we did not use the same method for giving the iodine, and that our procedure of giving occasional saturation doses of sodium

THE EFFECT OF IODINE PROPHYLAXIS  
ON THE INFANT THYROID

MATERNAL THYROID	SODIUM IODIDE			IODINE SALT			NO IODINE		
	NO. OF INFANTS	ENLARGED GLAND		NO OF BABIES	ENLARGED GLAND		NO. OF BABIES	ENLARGED GLAND	
		NO	PERCENT		NO	PERCENT		NO	PERCENT
NOT ENLARGED	50	9	18	121	4	3	79	40	50
SLIGHTLY ENLARGED (ENDEMIC COLLOID)	53	14	26	78	4	5	60	28	47
ADENOMATOUS GOITER	30	3	10	16	1	7	10	5	50
LARGE COLLOID GOITER	37	14	38	28	2	7	12	7	60

Fig. 10.—The effect on the infant thyroid of iodine given prophylactically to the mother during pregnancy.

iodide may not be adequate. None of our patients who depended upon iodine salt exhibited any hypertrophy of the thyroid, but the series is too small to be significant.

In no instance, except possibly Case 60, was there any indication that the use of iodine had done harm, and our experience during the past seven years has failed to develop such cases. However, in view of the experiences of Mussey, Plummer, and Boothby<sup>4</sup> and of Falls,<sup>9</sup> this possibility must be admitted and adequate precautions taken to avoid serious consequences, but we cannot believe that it should be used as an argument against the use of iodine routinely in pregnant women. We believe that the amount of good to be derived from such prophylactic medication by both the mother and her infant more than balances the possible harm in the occasional patient.

The protective effect upon the fetal thyroid of iodine administered to the mother during gestation adds a considerable argument in favor of such prophylaxis.<sup>10</sup> Among a group of more than 500 consecutive pregnancies studied clinically, the observations upon the condition of the infant thyroid were made as shown in Fig. 10.

Such a tabulation shows that without prophylactic iodine approximately one-half of all babies born in a region of endemic goiter will show some thyroid enlargement, but that under any form of iodine administration the incidence is considerably diminished, with iodine salt being, apparently, particularly effective.

#### CONCLUSIONS

1. The basal metabolic rate shows an increase during normal uncomplicated pregnancy of approximately 15 per cent, with a fall to normal in the first few days after delivery. A greater rise with slower fall to normal suggests increased thyroid activity incident to pregnancy.

2. A small percentage (in our series 20 per cent) of women with clinically normal thyroid glands have a metabolic rate which rises above plus 20 per cent. Patients with palpable thyroid disease show a greater tendency toward such high rates, the incidence rising to 35 per cent with small colloid and adenomatous goiters, and to 50 per cent in the large colloid type. This is taken to indicate that pathologic thyroid glands are less able to respond normally to the demands of gestation, but tend to function abnormally and so to produce symptoms of hyperthyroidism.

3. Iodine, given prophylactically during pregnancy, is apparently unable uniformly to prevent gestational hypertrophy of the normal thyroid gland, but seems to be quite effective in preventing such a change in glands which are pathologically altered when pregnancy begins, and may actually lead to a reduction in the size of certain colloid goiters.

4. Iodine given to pregnant women acts very effectively to prevent the appearance of congenital goiter in the newborn.

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## HOOKWORM DISEASE AND PREGNANCY

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**H**OOKWORM disease, caused by *Ankylostoma duodenale* or by *Necator americanus*, is found, according to Dock and Bass,<sup>1</sup> in all parts of the tropics, in many subtropical countries, and also in some temperate regions. It has, in all probability, existed from time immemorial, though its exact identity has been established and the causative agent isolated only in the past half century. It is characterized chiefly by an anemia of varying intensity, dependent upon the severity of the infection, with a concomitant state of mental and physical languor, rendering the subject more or less incapable of performing properly his appointed tasks, and hence is directly responsible for a great deal of economic inefficiency and waste. It is essentially a soil pollution disease, and thus affects particularly those whose work brings them into intimate relations with the soil, such as farmers and farm laborers, miners, etc. In our country it is found chiefly in the southern states, and in some areas it is responsible for severe economic losses. Some patients are heavily infected and are incapacitated, the majority have mild or moderate infestations and are not acutely ill, but are tremendously handicapped, while those with very light infestations are of considerable importance as carriers.

The disease may be contracted by ingestion of the ova with the food, but it is well established that the chief route of infection is through the skin, generally that of the feet, the initial lesion being commonly referred to as "ground itch." Going barefoot in infested areas is hence the usual way in which the malady is acquired. The infested mud is particularly prone to lodge between the toes; the encysted larvae dig their way into the skin and deeper tissues, reach the blood stream, then are carried to the right heart and thence to the lungs. Here they are entrapped in the capillaries because of their size, penetrate the tissues, and get into the bronchial tubes. Next they reach the mouth and pharynx, being carried there by the constant outward current of the mucous membrane or by coughing, and are swallowed. An astute Mexican observer, P. H. Lira,<sup>2</sup> has described this cough as a symptom of hookworm disease, and has reported cases erroneously diagnosed as tuberculosis in this stage of the infection. Dock and Bass also mention this cough as one of the symptoms. Reaching the small intestine, the larvae undergo further metamorphosis, and anchor themselves by means of their hooks, to the mucous membrane, chiefly of the duodenum and upper jejunum. Loss of blood ensues from the bites of the

worms; some of this blood is ingested by the parasites, some can be found in the feces by appropriate tests. There is some evidence suggesting that the worms also feed on intestinal mucus and on the mucosa. Bacterial infection of the bites occurs, and plays an important part in the pathology of the disease. Some observers believe that a specific toxin is in some way elaborated and absorbed. Ova produced by the female worms are constantly being cast off, but do not hatch into larvae in the intestine of the host; this occurs in the warm, moist soil after the eggs are passed in the feces. The persistence of the disease is maintained in great part by reinfection; Chandler<sup>3</sup> believes "that there is a rapid loss of the parasites and an equally rapid replacement by new ones." Both he and Bass believe, however, that some parasites may live in the intestine of the host for as long as six or seven years. One of my patients had been living in the city for five years, with little or no opportunity for reinfestation in the usual manner, but still harbored the worms.

The symptomatology naturally varies with the degree of the infestation. The severe cases present objective symptoms, the milder ones frequently do not, so that these patients do not realize that they are subnormal, hence many individuals of this type are overlooked unless one is on the alert. The mass surveys that have been made in this country and in others have revealed that in some localities 50 per cent or more of the inhabitants have been infected, with only a small proportion actually complaining of the subjective symptoms of the disease. Anemia is the chief characteristic, the hemoglobin being 30 per cent or less in the severe cases. The patients have a peculiar sallow, muddy complexion, differing from that of pernicious anemia or of ordinary secondary anemia. In the advanced stage we may encounter edema of the feet and legs, dyspnea, a hemic heart murmur, and at times albumin and casts in the urine, so that a mistaken diagnosis of cardiovascular disease may easily be made. The patients do not perspire so freely as do normal individuals. If the infection is acquired in childhood, as is common, growth is abnormally slow and the patient is "stunted," the hair development is scanty, the appearance of the secondary sexual characteristics is delayed, and in girls, as pointed out by Stiles,<sup>4</sup> the establishment of menstruation is retarded and it tends to be scanty and irregular. No definite information as to a possible increase in the percentage of sterility is available. Stiles, in 1910, on a visit to New Orleans, called our attention to some characteristics of the hair. It is frequently of an indefinite sandy color, neither blond nor brunette, is deficient in oil, and hence of a peculiar dull, dry appearance. This, with the rather characteristic anemia, has often led me to make a tentative diagnosis on inspection alone. The blood shows the usual picture of secondary anemia, plus an eosinophilia of varying intensity. The

final diagnosis, of course, is made by the finding of the ova or the worms in the feces. Two or three examinations may be necessary, and at times special concentration methods are employed.

Naturally, many thousands of pregnant women have suffered from this complaint, yet comparatively little attention has been paid to this combination, either by obstetricians or by public health workers. It goes without saying that a condition which may so profoundly affect a woman's general health would exert its influence on her reproductive life. Lambert,<sup>5</sup> writing of his experience with the disease in the Fiji Islands, states that in pregnancy "the dire effects of hookworm disease are dramatized most vividly," and is of the opinion that in this region there occurs each year, from this cause, a number of deaths of mother or child, or both. Dock and Bass state that "abortion is likely to occur, and it, as well as birth at term, may be fatal in anemic patients; lactation is imperfect in hookworm patients, but improves promptly under thymol treatment; the offspring of hookworm patients are likely to be poorly developed and marantic." And again, "When hookworm patients become pregnant, the tendency to dropsy is very much increased by the disease, and in severe cases the swelling is often great. The swelling of the labia is especially troublesome as the patient approaches term."

Cinselli,<sup>6</sup> in 1878, reported the case of a woman dying of putrid infection after delivering a dead baby. Autopsy showed marked anemia and hookworm infestation. Cinselli thought that the uncinariasis so lowered her resistance that the puerperal infection could not be combated. Bruni,<sup>7</sup> in 1891, reported a patient with marked anemia due to hookworm disease (diagnosed only the day before death), who died a few weeks after the delivery of a normal child. Tridondani,<sup>8</sup> in 1900, reported ten cases of severe hookworm disease in pregnant women, only one of whom went to term. Six of the others spontaneously delivered prematurely, and in three instances premature labor was induced because of maternal indications; one of these three mothers died on the eighth day of the puerperium, and one on the twenty-sixth. Six of the babies were lost, one being stillborn, the others dying shortly after birth. He thought that the loss of the infants was due partly to the anemia, the hydremia, and the anoxemia, but chiefly to a toxic action of the parasites, possibly to a specific toxin elaborated by them. Pinetti,<sup>9</sup> in 1899, reported a case terminating in premature delivery at seven and one-half months; he felt that this outcome was due to a specific toxin, to which the patient had not had time to adjust herself, as she had been infected for only two months. He quoted Mangiagalli,<sup>10</sup> who reported a patient in much worse general condition who did not deliver prematurely, probably because she had had time to adapt herself to the gradually developing toxemia. Raineri's<sup>11</sup> patient had a severe double infection with hookworm and bothriocephalus; she delivered a living, premature baby at the seventh month. Bolli,<sup>12</sup> in 1905, reported the case of a woman with severe infestation and delivery at term of a child weighing 2800 gm. He found that the blood of this child was subnormal in many respects as compared to the blood of a normal newborn infant. Sacchi,<sup>13</sup> in 1909, found 38 patients with ankylostomiasis in the course of a routine study of the feces in a series of 200 pregnant women; 37 of these 38 occurred in the 152 peasant women of the series, an incidence of 24.34 per cent, showing that the disease was at that time common among the

country people of Italy; the rice growers were particularly liable to the infection. His cases were mild or moderately severe, and did not show the heavy incidence of premature interruption of pregnancy noted by Tridondani. There was spontaneous or induced abortion in three instances, six patients delivered prematurely, and in one patient it was found necessary to induce premature labor because of renal damage. Eight of these 10 patients suffered from nephritis in varying degrees (fatal in one instance), two had severe chronic bronchitis, and the majority of these 10 had developed various other debilitating conditions before or during their pregnancies. Hence he felt that the hookworm infestation was only a contributing factor, but one of considerable importance in some instances. Sinnetamby,<sup>14</sup> of Ceylon, in 1905, related some experiences with a series of 32 pregnant women who were seriously ill because of this complication. There were six maternal deaths, due, he felt, to cardiac failure subsequent to dilatation of the heart caused by the anemia. He stated that premature labor was the rule, but gave no details. Wilson,<sup>15</sup> of South Carolina, in 1918, reported three cases, two with associated toxemia; there was one fetal death on the twelfth day postpartum. Isfrán, of Paraguay, in 1926, in the course of the mass treatment of 100,000 persons, encountered 205 pregnant women who volunteered the diagnosis of pregnancy complicating their hookworm infection. He felt sure that many other such patients were also treated, in whom the pregnancies were undiagnosed. Soper<sup>17</sup> treated 63 women who were from two to eight months pregnant.

The incidence of renal lesions in severely infected pregnant patients is high, as noted by these various observers, and is generally thought to be due to a specific toxin elaborated by the parasites. The occurrence of eclampsia in hookworm patients has been reported by Rowan,<sup>18</sup> of Mississippi, Turberville,<sup>19</sup> of Florida, and Opocher,<sup>20</sup> of Italy. Rowan stated that southern Mississippi, at the time of his report (1911), was a highly infested area, and that the native white women were peculiarly subject to the toxemias of pregnancy. In 19 cases of eclampsia he could eliminate only 2 as being possibly free from hookworm disease. A number of his patients who were treated for this complication had no trouble in subsequent pregnancies. Kitrell, in discussing this paper, stated that he knew of several instances in which the combination of hookworm disease and pregnancy resulted in the death of the mother from convulsions. Turberville felt that hookworm infestation, by preparing the ground for the operation of the causative factor, had an indirect rôle in the abnormal frequency of eclampsia in his section of Florida. He encountered 7 cases in 300 pregnant women, while 2 neighboring physicians reported incidences of 6 to 200 and 15 to 350, respectively; the average ratio being estimated as about one to 500. The author felt that he had in several instances prevented the development of eclampsia by the eradication of the hookworm infection; one patient developed eclampsia before the treatment could be completed, and in another instance the combination resulted in the death of the patient. In Opocher's patient eclampsia supervened in the seventh month of the first pregnancy; labor was induced, thymol was administered, and a macerated fetus was delivered.

For several years, in a rather casual manner, I have watched for patients presenting clinical manifestations of hookworm disease in my obstetric service at the New Orleans Charity Hospital, and up to January 1 of this year I had thus detected 22 cases, each diagnosis confirmed by stool examination. Since that date, I have had a routine examination of the feces made on each patient admitted, and have thus discovered 12 infected women out of a total of 180 admitted. On one occasion there were four such patients in the ward simultaneously. All of these

patients were from the country, primarily or secondarily, the three now living in the city having come from the rural districts in the past two to five years. On this basis of a 6.7 per cent incidence, we should have had 41 cases among the 616 patients cared for by the service in 1928, instead of the seven actually detected during that year.

Many of these 34 patients had light infestations, and some might be designated as carriers, though even the carriers are somewhat subnormal, as noted by Dock and Bass. A few were severely infected, as shown chiefly by the anemia; thus, of the 19 patients on whom blood counts were made, the total red count was 3,000,000 or less, with the hemoglobin between 25 and 50 per cent in 11 instances, and in two of these it was less than 1,000,000. Nine of the 34 patients had toxemias of varying degrees of severity, and 8 of these 9 were in the above group characterized by marked anemia. In addition, one patient admitted one month after delivery with puerperal parametritis and hookworm disease gave a history of antepartum eclampsia. Of three eclamptic patients recently studied, one, from the country, was found to be heavily infected; ova of *Ascaris lumbricoides* were also found. The other two, one from the country and one from the city, were free from this complication. I would expect negative findings in my eclamptic patients, as these women are generally urban, because of the difficulty of transporting such patients from more or less distant points. These findings are in accord with those noted above, and it would appear that severe hookworm disease does predispose to the toxemias of pregnancy, possibly through the action of a specific toxin, but more probably because of the very poor general condition of the patient.

There were only 3 spontaneous interruptions of pregnancy in this series, probably because the majority of the patients were not severely infected. Two patients were very anemic, one had a red cell count of less than one million, with general edema; the other had a red count of 1,170,000, and was toxic, with a systolic blood pressure of 162. Both delivered at the seventh month. The other patient was the one suffering from eclampsia; she also delivered at the seventh month. These babies were stillborn. Several of the babies born at term were smaller than normal, but otherwise were apparently healthy.

As it is clear that this complication affects the pregnant woman unfavorably, and may in severe cases cause the loss of the child, it has been my policy to treat these patients along accepted lines. Thymol, 3 to 4 gm., in divided doses, preceded and followed by a purge of magnesium sulphate (not castor oil), has been used in most instances. It is important that no oily substance of any kind or alcohol in any form be taken for the first eight to ten hours after the thymol, because of the danger of absorption of the drug in these media. Dock and Bass state that thymol may produce premature labor, and hence should not be used in pregnancy, but this has not been my experience, and Dr.



Bass tells me that this statement was based mainly on theoretic considerations. Carbon tetrachloride, in 3 c.c. doses, together with 30 to 40 gm. of magnesium sulphate, was given to some patients. Soper and Isfrán used this drug in doses of 2.4 c.c. The usual treatment at present employed in hookworm eradication campaigns is a mixture of carbon tetrachloride and oil of chenopodium, the best proportions, according to E. C. Faust, Professor of Parasitology, Tulane University,<sup>21</sup> being 1.8 and 0.7 c.c., respectively. Lambert states that oil of chenopodium is claimed by some to be contraindicated in pregnancy, but in Isfrán's opinion this idea is erroneous. If carbon tetrachloride is used, it is highly important that it be absolutely pure. Lambert treated 42,000 persons with this drug without untoward developments, but in the next 8,000 he had three deaths, due to impurities in the preparation used. At present, in the Charity Hospital, thymol is preferred, because of the occasional occurrence of toxic manifestations following the use of carbon tetrachloride. The treatment, whatever drug be used, should be repeated several times, as one treatment usually fails to remove all the parasites. It is well to check the thoroughness of the treatments by repeated stool examinations. Reinfestation is very common, hence the patient should be cautioned as to its possibility, and should be instructed as to the methods to be pursued in avoiding its occurrence.

Practically all observers agree that treatment during pregnancy does not cause abortion or premature labor. Lambert stated that he had treated hundreds of pregnant women with carbon tetrachloride with no abortions as a result. Isfrán, as well as Soper, had similar experiences. The former noted five abortions occurring from eight to twenty-nine days after treatment in the 63 cases followed up by him, but did not think that the drug was responsible for any of these interruptions. In Soper's series of 63 cases, two abortions occurred on the tenth and twelfth days, respectively, but the author did not think that these occurrences were due to the treatment. My experience has confirmed these observations, and the majority of my patients were treated so soon as the diagnosis was made, with no deleterious effect on the pregnancies. The three spontaneous interruptions of pregnancy, noted above, occurred in untreated patients, delivering shortly after admission, before the diagnosis was made. It would appear that treatment should tend to prevent these spontaneous premature deliveries that are liable to occur in the severer cases.

It is evident, then, as recently stated by Gamble,<sup>22</sup> that hookworm infestation is still a public health problem in the southern states, though the surveys and mass treatments so diligently pursued have reduced the percentage of infected persons markedly. Its occurrence in conjunction with pregnancy is not at all uncommon, as is shown by the fact that, in a city hospital, I easily detected these 34 cases. There

can be little doubt that this disease predisposes to the development of toxic states in severely infected pregnant women, and that it is a potent factor in increasing the percentage of premature interruptions of pregnancy in such patients. Treatment along accepted lines is well borne, does not cause interruption of pregnancy, and is of distinct benefit to both mother and child.

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MAISON BLANCHE BUILDING.

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## TRICHOMONAS VAGINALIS, DONNÉ

### SECOND REPORT OF EXPERIMENTAL AND CLINICAL OBSERVATIONS

BY CARL HENRY DAVIS, M.D., F.A.C.S., MILWAUKEE, WIS.

A REPORT on a six months' study of *Trichomonas vaginalis* was submitted to the *Journal American Medical Association* for publication in June, 1928. Today we wish to add a brief summary of the observations made since that date. The experimental work was done at Columbia Hospital with the cooperation of Miss Charlotte Colwell.

#### I. CLINICAL OBSERVATIONS

Routine microscopic examination of diluted fresh vaginal secretions has led to a diagnosis of *Trichomonas vaginalis* vaginitis in 50 private patients during an eighteen-month period. *Trichomonas vaginalis* has not been found in a single patient who has been entirely free from symptoms of leucorrhea or vaginitis. However, a number of women had been able to keep the condition under control by douching one or more times each day. The duration of symptoms has varied from a few days to more than seven years. Most of these patients had been previously subjected to a variety of treatments ranging from antiseptic douches to hysterectomy. One girl who had had vaginitis for seven

years gave a history of 3 vaginal operations, and shortly before my examination a hysterectomy had been advised elsewhere. Only 3 pregnant women in approximately 150 examined had *Trichomonas vaginalis* and 2 of these were cured during the pregnancy. The third had many parasites at the time of delivery and still has the infection as she has been unable to return for adequate treatment.

A review of the literature shows that a number of writers do not consider *Trichomonas vaginalis* pathogenic. This belief probably explains the indifferent attitude of most gynecologists. The rarity with which this condition has been diagnosed is due to the fact that diluted fresh vaginal secretion is not considered an essential part of a gynecologic examination. Observations made during the past eighteen months have convinced me that one should not depend on stained slides and neglect the information which is so easily obtained from the examination of fresh secretion. Furthermore, I am convinced that with few exceptions *Trichomonas vaginalis* rather than the associated bacteria are the cause of the very annoying vaginitis with which these parasites are associated. All acute symptoms are usually relieved within a few hours after a treatment which kills most of the trichomonas. Unless some form of treatment is continued at frequent intervals there is always a prompt recurrence of the irritating discharge and acute symptoms of vaginitis when the trichomonas increase sufficiently in number. Permanent relief has been secured in every patient whose infection with *Trichomonas vaginalis* has been cured. Culturally these flagellates will not show evidence of growth unless human blood serum is present in an adequate amount in the medium. Growth in the vagina appears to be most rapid during the menstrual period when an excess of blood is present. At other times they are associated in the diluted fresh secretion with large numbers of leucocytes.

The pus cells decrease rapidly and largely disappear in most cases within a short time after it is no longer possible to demonstrate trichomonas. Reappearance of the flagellates in considerable numbers is always accompanied or soon followed by large numbers of pus cells in the vaginal discharge. It is, therefore, my belief that *Trichomonas vaginalis* is a pathogenic flagellate and the specific cause of a most annoying and persistent vaginitis.

Thus far it has not been possible to determine the source or method of infection in a single instance. A number of histories indicate some relation to coitus and rarely trichomonas are observed in the urines of men patients at the hospital. However, I have examined the urines of many men whose wives had *Trichomonas vaginalis* without finding flagellates. Lewis and Carroll reported the finding of trichomonas in the pelvis of both kidneys, bladder, and vaginal secretions of a patient. Once urologists begin to look for this condition it is probable that other cases will be found. Direct implantation of *Trichomonas vaginalis*

appears necessary since these flagellates die so quickly under unfavorable conditions. Nevertheless I have been unable to determine the source of contact and no two cases have come from the same household. It has not been possible to test routinely the feces of these patients but trichomonas have not been found in the few examined.

Examination of vaginal secretion should be made immediately after a period or after the patient has not douched for forty-eight hours.

#### TREATMENT

*Trichomonas vaginalis* may be killed by a variety of antiseptics and various methods of treatment. In our first report the relative killing effects of various drugs were shown. They may be killed by drying, heat, and by a sufficient degree of cold. It is believed that drying and heat may be used effectively if combined with other methods of treatment. Theoretically it should be possible to eliminate *Trichomonas vaginalis* from the vagina with a single thorough treatment. It is frequently difficult or impossible to demonstrate a single trichomonas forty-eight hours after a thorough treatment, but following a period they may be present in great numbers although none could be found just before menstruation. It would seem that these flagellates must be harbored in inaccessible places as under the inflamed and thickened vaginal mucosa, or possibly in the cervical canal. Treatment must be continued at frequent intervals until all pus and blood have disappeared. It is also necessary to reexamine the patient immediately after the menstrual period for several months before she may be considered cured.

The following plan of treatment is now being used with some success for the group of patients who have had more than one relapse following an apparent cure. At least three times each week the vagina is thoroughly cleansed with liniment of soft soap. After the excess of soap is removed an antiseptic powder is blown onto the cervix and vaginal vault. On other days the patient uses a hot douche containing liniment of soap or compound solution of cresol. A special douche tip permits thorough distention of the vagina. Office treatments are continued during menstruation since that is the time when the relapse seems to occur. Icthyol glycerine tampons are of value during the acute stages of vaginitis, but they appear to be of little value in these chronic cases. It is believed that every case can be cured with persistent treatment although it may require many months for some.

#### II. EXPERIMENTAL OBSERVATIONS

After many experimental attempts to grow *Trichomonas vaginalis* in an artificial medium, we obtained a satisfactory growth in Locke's solution to which approximately 5 per cent of whole human blood had been added. Later it was found that a like amount of relatively fresh

human serum could be substituted for the whole blood. Dextrose broth with 5 per cent human serum appeared to be a better medium than the Locke's solution provided the  $P_H$  was similar to that of human blood. The trichomonas seemed to grow best and remain active longest in tubes containing 15 to 20 c.c. of the medium. Using this type of medium eight strains of trichomonas were successfully grown during the spring of 1928, and carried through a varying number of subcultures.

A new cultural study was started October 13, 1928, in glucose serum bouillon containing 5 per cent human blood serum. Transplants were made every two, three, or four days, usually to the same medium; occasionally switching to a Locke serum medium. The trichomonas continued to grow actively in every transplant until the night of December 21 when an accident to the mechanism of the incubator regulator caused the temperature to rise to 50° C. or higher (the thermometer registers only to 50° C. or 121°F.). Of the six subcultures of trichomonas in the incubator none were alive in the morning. Bacterial cultures subjected to the same temperature were unharmed.

Following the loss of this culture, which had been carried to the twenty-third transplant, we inoculated eight additional strains in the same type of medium but there was no growth. These specimens had been inoculated in a small amount of glucose bouillon or Locke's solution at the office and a few hours later transferred to the culture medium at the Columbia Hospital laboratory. In each case the trichomonas appeared rather inactive when inoculated and the following day had apparently disappeared.

A new culture was obtained from an untreated patient by inoculation directly into Locke's serum medium on March 15, 1929. Twenty-five days later this was killed by excessive heat in the incubator. It had been carried to the seventh transplant. More recent attempts to grow trichomonas from treated patients have been unsuccessful. A few have grown actively in the first transplant but have disappeared in the second or third.

Morphologic studies of *Trichomonas vaginalis* have been made by a number of observers. Among the best descriptions are those given by Lynch in 1915 and Hegner in 1925. The later study was made from smears which were fixed in Schaudinn's solution and stained with Heidenhain's iron harmatoxylin. We have not attempted a study of stained specimens, but by means of dark-field illumination we have confirmed in most respects the published descriptions. The size and shape of *Trichomonas vaginalis* vary markedly in different strains and at times in the same one. This is due in part to the rapidity of growth and cell division. A healthy trichomonas is somewhat pear-shaped. Four flagella arise from the anterior end of the organism as two pair, each with a common attachment. There is a tail-like protrusion at the

other end, which apparently is used as an anchor. During life the flagella appear to be in motion at all times. In dark-field studies the movements of the undulating membranes may be followed, but this is not seen in ordinary observations under lower magnification.

Trichomonas which are slowly dying in an old culture become spherical and are covered with many bacteria. It would appear from the large numbers attached to these feeble organisms that bacteria may be the cause of their death. Trichomonas which are experimentally killed slowly as by warming the culture to above 46° C. for ten minutes, also become round or slightly oval and resemble large leucocytes. If killed suddenly by glycerine or alcohol the shape is not changed.

From time to time we have observed masses of what may be dead trichomonas or some sort of cyst formation. It has not been possible to grow trichomonas in a subculture from a tube in which the active organisms disappeared and the cyst-like forms appeared.

Andrews in 1926 reported that *Trichomonas hominis* is killed in solutions heated to 48° C. for ten minutes. Using this as a basis for treatment Lewis and Carroll report the cure of a case of *Trichomonas vaginalis* vaginitis with diathermy. Believing that there might be some difference in the thermal death point of *Trichomonas vaginalis* and *Trichomonas hominis* we tried the following experiment: A small amount of an actively growing culture was placed in a small thin-walled test tube and held in a water-bath for ten minutes. At the end of this time a drop was examined under the microscope and the rest inoculated into our regular serum culture medium which had been previously warmed by placing in the incubator. Tubes were also placed in the ice box to determine the effect of cold.

THERMAL DEATH POINT OF TRICHOMONAS VAGINALIS

TEMPERATURE		WATER-BATH 10 MIN.	ACTIVITY IN DROP	CULTURES
CENTIGRADE	FAHR.			
42°-43°	108°	“	Very active	No cultures made
44°-45°	113°	“	Slight activity	No growth
46°-47°	115°	“	in clumps	No growth
48°	118°	“	None	No growth
9°	48°	Ice box	Very active	Growth active
		12 Min.		
9°	48°	Ice box	None	No growth
		24 hr.		
Control in incubator				Active growth

Results shown in the above table indicate that 46° C. + for ten minutes will kill *Trichomonas vaginalis*. It is apparent that they may also be killed by cold.

Our experimental observations show the need of an intensive study of *Trichomonas vaginalis*. Data on each culture must be much more

complete than in the past. So far as possible the life history of each strain must be worked out. We should record the name of the person from whom the blood serum is obtained as well as the host of the *Trichomonas vaginalis* strain studied.

Both experimental and clinical evidence suggest that the virility of these flagellates varies at different times and that they may be killed more easily during the late winter and early spring. In another year it may be possible to state this more definitely.

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141 EAST WISCONSIN AVENUE.

### A PRELIMINARY REPORT ON TEMPORARY ROENTGEN-RAY CASTRATION IN THE TREATMENT OF SUBACUTE ADNEXAL INFLAMMATION

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(From the Service of the Long Island College Hospital)

IT IS now an accepted principle that there is no operative treatment for acute salpingitis for, unless a local abscess forms in the culdesac which admits of vaginal drainage, the management of this type of infection is essentially medical. *Only the "cooled case" should be operated upon, and then operation is not done for cure of the infection, but for the relief of symptoms traceable to the resulting pathology.* Rest and time usually effect a symptomatic cure. In support of this statement Holtz reports that in more than 1000 cases of acute salpingitis treated by purely expectant methods, a clinical cure was recorded in 82 per cent, while 12 per cent had functional cures with resulting conception (in only 2 per cent was there absolute failure) and such results are being duplicated in almost every clinic.

In a study of the case histories of patients with this disease, admitted to our clinic in the past five years, fully 70 per cent may be classed as gonorrheal. These women gave a history of recent marriage or illicit coitus followed by skenitis, bartholinitis, or endocervicitis. This is a larger percentage than has been credited to Neisserean infection by most observers. Eighteen to 20 per cent were traced to a non-specific origin, pelvic lesions following postabortal or puerperal infection; while 5 to 7 per cent were tuberculous. This ratio of incidence cannot be checked up by bacteriologic findings, for many women who marry men suffering from a chronic gleet contract an infection

but pass through such a mild type of cervical and urethral inflammation that the profuse discharge loaded with gonococci is absent at the time that they present themselves for treatment.

Whether the infection is of specific or nonspecific origin, the pathology is much the same, i.e., an extension of the inflammation from the endometrium to the endosalpinx, always bilateral, though the severity of the infection and the tissue reactions may be greater on one side than on the other. Formerly it was taught that in gonorrheal infection the extension was always bilateral, while in septic cases following operation, abortion, or childbirth, the invasion was through the parametrium and usually only one tube was involved. Repeated autopsy studies with serial sections of the uterus and tubes have shown that any infection which extends from the endometrium involves the endosalpinx of both tubes. Likewise, all tubal infections tend to subside spontaneously. The gonococcus cannot exist without oxygen and once it has been encapsulated by tissue reaction, its death is inevitable and activity ceases. The recession of bacterial activity and the evidences of clinical improvement are always coincident.

Curtis states that gonorrheal salpingitis is a self-limited process and that the exacerbations are in reality fresh infections either from operative extensions from an infected lower genital tract, such as an infected cervix, or from the male. To this, we can in part subscribe, for in our experience pelvic and sexual rest in time always effect a symptomatic cure; this, however, may be expedited by temporary castration producing a suspension of the periodic menstrual engorgement. The exacerbations in temperature and leucocytosis occur at the menstrual period and are explained by the fact that the cervix is open during menstruation and the protecting mucus is washed away by the menstrual flux, while the menstrual blood and clots act as excellent culture media. Skene's tubules often remain as infective foci and should always be destroyed. The gonococcus does not live long in the lumen of the tube, though it has been assumed that the bacteria remain viable in the deeper structures of the tubal wall. This last impression has been disproved by Curtis, for his study of over 200 thoroughly ground fallopian tubes reveals the fact that it is almost never possible to obtain the gonococcus (by culture) longer than two weeks after the disappearance of fever and leucocytosis. This observation coincides with the clinical picture of this form of infection—and were it not for coitus and the recurrence of menstruation, absorption of the products of tissue reaction would go on rapidly. The effects of sexual trauma must not be underrated, for clinical experience has shown that most careful bimanual examination will break down barriers and excite cellular activity in the "uncooled" case; hence, coitus must have a similar effect.



When the organisms are nonspecific, more or less of a similar condition exists. The acute attack tends to subside, and the exudate is absorbed in the same way as though a specific organism were present. The difference, however, is in the fact that nonspecific organisms may be anaerobic. This permits the inflammatory reactive processes to quiet down, but the retained organisms may retain their virulence and have a decided potentiality for harm.

The life of the buried streptococcus has never been definitely settled, for it has been isolated from the tube as late as ten, twelve, and nineteen years from the original attack. This makes operation always more hazardous when there is a history of septic infection. In both types of infection autosterilization occurs, and the woman recovers by developing her own immunity which protects her against the bacterial invasion that has taken place. The only difference is that the organisms in specific infections have a limited life history, while those of nonspecific infections retain their activity for an unknown period of time. The cardinal principle of treatment is rest in bed for days or weeks. Pain is relieved by codein and aspirin, the therapeutic light, or the ice bag, whichever gives most comfort to the patient. The lower bowel and pelvic colon are kept empty by small enemas. Body resistance and elimination are maintained by small repeated blood transfusions, hypodermoclysis, and intravenous infusions of glucose while tissue reaction is stimulated by protein injections and vaccines. Menstruation and the resumption of marital relations frequently relight a quiescent process, for pelvic and sexual rest are the basic factors in treatment. We operate for the results of infection; when, therefore, should operation be done?—how long should it be delayed?

In 1908, F. F. Simpson presented before this Society his results in the conservative treatment of 400 cases of acute adnexal infections. At that time he laid down the principle that no patient should be operated upon until the temperature has been normal night and morning for a period of at least two weeks; that the leucocyte count must be below and remain below 11,000; that the "poly" count must be 75 per cent or less, and that pelvic manipulation, as bimanual examination, should not cause a rise in the temperature or in the leucocyte or "poly" count. To these requirements we have added that the exudate must be hard and insensitive and show evidence of being absorbed; and that the blood sedimentation time must be ninety minutes or more. These conditions, when they obtain, prognosticate a good surgical recovery and allow conservative operations which permit the retention of the menstrual function. Experience has taught us that there is no exception to these minimum requirements. All of this takes time and as Miller so aptly puts it, "the wise surgeon is the one who waits and continues to wait until the patient by her immunity has overcome the infection."

Rest in bed, the therapeutic light, the ultraviolet ray, diathermy, hot vaginal douches and vaginal packs have all been credited with aiding the organization and absorption of pelvic exudates, but the greatest of all is time. The recurrence of menstruation always activates the process, causes a slight rise in temperature, produces an increase in the leucocyte count and increases the pain. Clinically we have noted in those cases of severe puerperal infection which are followed by prolonged amenorrhea that the pelvic exudate and the pelvic symptoms rapidly disappear. In line with this observation, in 1918, Dr. Beck and I operated upon a woman on a mistaken diagnosis and found the pelvis "too hot"; the adhesions were diffuse and injected, the tissues friable and edematous, and before going far with the procedure, we decided that, because of her youth, it would be better to close the incision than to remove her entire pelvic structures. This we did and because of a persistent metrorrhagia we subjected her pelvis to x-ray treatment. Nonsterilizing doses were used, but sufficient dosage was given to produce an amenorrhea which lasted for several months. The surprising thing about this case, was, that the exudate simply melted away, no further exacerbations ever occurred and the patient was clinically cured. Similar cases were treated in 1920 and 1921, but the real significance of this treatment was not brought to our attention until 1924 when Naujoks published his article on temporary sterilization in women suffering from pulmonary tuberculosis, and in 1926 when Gutman and Bott published their thesis suggesting temporary sterilization in the cure of adnexitis and parametritis. During the past five years we have treated 34 patients on these principles, i.e., producing a temporary x-ray castration after the first acute symptoms of tubal inflammation subsided. In this small series there were 16 cases of gonorrheal origin; 10 giving histories of previous abortion or labor, belonging to the puerperal class, and 8 which fell in the tuberculous group. The periods of amenorrhea ranged from four months to one year; in all the patients the pathologic exudate in the pelvis rapidly disappeared, the uterus became mobile, and the actual adnexal masses were easily defined. It is surprising when operating upon these women—and incidentally but few have needed operation—to find how free the pelvis is of adhesions and how easily existing ones are separated. Of the seven women operated upon, all had retrodisplacements with adnexa in the culdesac. The other twenty-seven had the uterus forward and have had complete symptomatic cures. In no case has menstruation failed to reappear, and one woman has become pregnant.

It will be argued that the same results can be secured by rest and time. To this I do not subscribe, for premenstrual, pelvic and abdominal soreness have been a more or less constant story in conservatively cured cases. This symptom has occurred right up to the time of the menopause when apparently all of the subjective symptoms seem

to disappear. On the other hand, in the cases treated by x-ray the premenstrual and peritoneal soreness was absent. The value of x-ray sterilization to our armamentarium has been best demonstrated in patients with tuberculous salpingitis, peritoneal extension, and persistent temperature. These patients show temperature reactions at each succeeding menstrual period. Furthermore, these patients usually have a leucopenia and a low sedimentation time—both evidences of poor resistance. Temporary x-ray sterilization has changed the picture in these women and has allowed hygienic and dietetic measures to do their work without handicap. We append a detailed technic for the roentgenologist and suggest that the best time to give this treatment is just prior to ovulation, for at this time the more mature follicles can be destroyed without injuring the primordial follicle. Very small dosage should be employed; this may be repeated if necessary at subsequent treatments.

While our series is too small to draw any definite conclusions, I believe that by the employment of this simple means of treatment we can shorten the convalescence period in tubal infections, conserve the adnexal function, and save many women from mutilating operations.

#### ILLUSTRATIVE CASE HISTORIES

I have selected four cases which I believe are so typical that they will prove my point. Skene's glands should be destroyed as a preliminary in all gonorrheal cases.

CASE 1.—Mrs. B., twenty-four years old, married two months, noticed burning urination and profuse purulent vaginal discharge while on her wedding trip. She was in bed all of the week following the menstrual period, complaining of severe lower abdominal pain and fever. On entering the hospital, two weeks after marriage, she presented the clinical picture and signs of an acute gonorrheal infection of Skene's glands, cervix, uterus, and both tubes. She was put to bed and treated expectantly. In fifteen days her temperature was normal, the discharge was mucopurulent, and well-defined masses could be outlined on both sides of the uterus. She was treated with the therapeutic light, milk injections, and the violet ray. All of her symptoms tended to improve, only to light up with the occurrence of menstruation. Furthermore, these symptoms recurred at the succeeding period, notwithstanding the fact that she had not resumed her sexual life. After the second exacerbation she received two x-ray treatments which checked her menses for four months. Absorption continued and the pelvis was free from any demonstrable pathologic condition. Early in 1927, she divorced her former husband and married again. Considering herself perfectly well, she wished to become pregnant. Insufflation demonstrated her tubes to be closed. She was operated upon and, the fimbria and adhesions were freed on one side, while the opposite tube which showed nodular obstruction was removed. Her complete relief from premenstrual pain and abdominal soreness was marked.

CASE 2.—Mrs. D., aged twenty-one, married, became pregnant and contracted specific infection at the same time. As her husband did not want children, she had an abortion performed at the sixth or seventh week. She was very ill on admission to the hospital; temperature 104° F.; pulse 130; marked abdominal

distention and tenderness, with a diffuse mass running from pelvic wall to pelvic wall. She was treated with rest, milk injections, and light therapy. In about ten days' time her temperature began to subside. When the menses recurred, all symptoms became exaggerated. Two x-ray treatments were given which were followed by an amenorrhea for six months with complete subsidence of pelvic lesions. This woman was examined and her pelvis found to be free from exudate; left ovary was cystic, the size of a hen's egg, and insensitive. Patient had no complaints.

CASE 3.—Mrs. Z., aged thirty, married and sterile. Examination of husband was negative. She complained of pre- and co-menstrual dysmenorrhea, leucorrhea, and menorrhagia. Examination showed a mild endocervicitis with a halo of erosion about the external os, and a retroflexed uterus with tuboovarian masses in both fornices. She ran an evening temperature of 100.4° F.; had a low leucocyte count and a sedimentation time of only forty-five minutes. The lungs were x-rayed and a pulmonary lesion was ruled out. After observation for a week, at the request of her husband who was a physician, we operated and found tubal tuberculosis with peritoneal extension; there was no free fluid, but miliary tubercles were scattered over both broad ligaments, sigmoid, and peritoneal covering of uterus. Both tubes and the cornua of the uterus were removed. Convalescence was uneventful until her menstrual period when she had temperature, peritoneal pain, tension and rebound. This was repeated at her next period. It was difficult to persuade her husband to allow temporary castration, but finally he consented. She was given two x-ray treatments just after her menses. There was an amenorrhea of eight months during which time her general condition improved, she gained weight, and her pelvic symptoms entirely subsided. On bimanual examination the uterus was found to be small and movable; the ovaries were free and palpable, and vaginal discharge had ceased. When seen in March of this year, menstruation was regular without pain and she considered herself cured.

CASE 4.—Mrs. F., aged twenty-one, married, was operated upon in February, 1927 in Newark for what was diagnosed as appendicitis. The appendix was removed and the ileum was found adherent in the pelvis; adhesions were freed with considerable bleeding so that the surgeon desisted from further exploration. The wound healed, but the temperature and pain in right side and pelvis continued. After consultation a vaginal incision was made in the right broad ligament. The convalescence was slow and attended with continuous evening temperature, loss of weight, distention, and periodic vomiting spells preceded by colic. This continued until she entered our service in November, 1928. At this time she weighed 90 pounds, was pale and pinched looking. She had an evening temperature of 102° to 103° F., and pulse 120 to 140; the abdomen was distended, and there was general tension but no rebound except in the left lower quadrant. Each day she vomited after an attack of intestinal colic, though enemas and Harris enteroclysis caused the free passage of gas. Pelvic examination showed a small uterus pushed forward and to the right by a mass in the left lower quadrant which involved the ovary, tube, and sigmoid. The attacks of pain and reversed peristalsis began in the left lower quadrant. She was transfused and treated with daily glucose infusions, the therapeutic light, and violet ray. For two weeks in each month the temperature was lower and her intestinal symptoms better, only to be activated for a week before and during each period. Gradually a large fluid accumulation formed in the culdesac. This was incised, evacuating a quart of serum containing tubercle bacilli. There was some local relief but no general improvement. I then persuaded her family to allow me to stop her menstruation with very mild repeated doses of x-ray. There was a gradual but complete cessation of symptoms. The exudate was absorbed, the temperature fell, and all of her intestinal symptoms disappeared.

From time to time her improvement has been continuous. When last seen in March, 1928, she had gained twenty pounds and her pelvis was free from any palpable pathologic condition.

My associate, Dr. A. L. L. Bell of our X-ray Department, has kindly supplied me with details of roentgen treatment in subacute pelvic infections with or without menstrual disturbances.

The dosage must of necessity vary in different cases owing to the variation in the distance of the ovaries from the anterior abdominal wall, and also to their distance from the skin surface posteriorly. The object of the treatment is to apply to the ovaries an x-ray dose of about 215 to 230 electro-static R-units (Duane-Glasser), using 180 to 185 K.V. and a filtration of 0.5 cm. of Cu and 1 mm. of Al. The ovaries are assumed to be 0.4 of the total depth of the pelvis from the anterior skin surface. In a patient whose total pelvic depth is 25 cm., the ovaries are calculated to be 10 cm. from the anterior skin surface and 15 cm. from the posterior surface. Using a depth dose chart, we find that at a depth of 10 cm. 35 per cent of the dose administered to the skin reaches the ovaries, and at a depth of 15 cm. between 32 and 35 per cent of the dose administered to the skin reaches the ovaries. Therefore, in treating such a patient, an area 20 cm. square anteriorly and posteriorly is given a dose of 320 R-units. The sum of the 35 and 33 per cent depth doses gives 217.6 R-units applied to the ovaries. These doses may be given at one time, but we usually administer them on successive days; there are no reactions from doses of this size, but we think it safer to divide them. In some cases where the infection is particularly active we have divided the treatments, so that only about 50 R-units (depth dose) are applied at one time. This dose is not repeated for at least two months, or until after the second menstruation following the first treatment. With these doses we have not produced any permanent amenorrheas.

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## ACUTE PUERPERAL INVERSION OF THE UTERUS

BY PALMER FINDLEY, M.D., OMAHA, NEB.

FOUR papers have appeared in the Transactions of the American Gynecological Society on this subject. W. H. Byford, in 1879, reported a case of chronic inversion; Edward P. Davis, in 1893, reported a single case of acute inversion; B. Bernard Browne, of Baltimore, in 1899, reviewed operative procedures; and Reuben Peterson, in 1907, discussed anterior colpohysterotomy in the management of chronic inversion.

Browne expressed the opinion that inversion of the uterus was probably more frequent in ancient times as judged from frequent references and accurate descriptions contained in the writings of Hippocrates, Araetius of Cappadocia, A. D. 30-60, Celsus, A. D. 1-50, Themison, B. C. 50, Rhazes of the eleventh century, and Ambrose Paré in the middle of the sixteenth century. That inversion of the uterus may well have been of more frequent occurrence then than now is supported by the methods then employed in delivery in the standing or kneeling position or in sitting upon a hollow stool. A more potent factor than that of position was the lack of means of expediting labor to prevent spasmodic exhaustion.

In 1847 Valentine de Vitry reduced an inverted uterus of sixteen months duration and from that time on we find numerous procedures devised for the correction of the lesion.

All writers on the subject refer to the extreme rarity of inversion. From the fact that the accident occurs more often in homes and in the hands of the incompetent, rather than in hospitals under skilled management, it is fair to assume that inversion is not so rare an occurrence as recorded statistics would indicate. As evidence of this assertion W. H. Fisher collected 38 unreported cases in the neighborhood of Toledo, Ohio, and adds that he was unable to make a complete survey.

I have seen four acute puerperal inversions of the uterus. The first was in a European clinic. A version and extraction had been performed; the placenta was delivered by forcible expression under general anesthesia when the uterus completely inverted. There was much loss of blood and extreme shock. An ineffectual attempt was made at reduction; this was followed without delay by a vaginal amputation. Two hours later a postmortem examination revealed the transfixion of a loop of bowel by sutures. Death was the probable result of shock from operation, superimposed upon the initial shock of the inversion.

Following is a brief history of three cases seen in consultation:

CASE 1.—Mrs. A., aged twenty-four years, primipara, was delivered by forceps of a full-term baby weighing 8 pounds. Failing to deliver the placenta by ex-

pression, the hand was introduced into the vagina. It was then that the inverted fundus was discovered. The placenta was removed and the vagina packed with gauze, but the hemorrhage was not effectually controlled. All means at hand were employed to resuscitate the mother, and help was summoned. I saw the patient some six hours later; she was in extreme shock and blood was oozing through the vaginal pack. We removed the pack and an ineffectual effort was made to reduce the inversion. A pack was again inserted, but this also failed fully to control the bleeding. With the able assistance of two surgical nurses and two doctors the fundus was amputated. A minimum of ether was employed; the operation consumed not more than ten minutes. This case occurred in a farmhouse where there were no facilities for blood transfusion. The patient died within a few hours.

CASE 2.—Mrs. B., aged twenty-seven years, primipara, delivered herself after a prolonged labor. The attending physician found difficulty in delivering the placenta and doubtless used considerable force upon a relaxed uterus. Following closely upon the expression of the placenta, there was profuse bleeding and shock, but this condition did not last long. The attending physician failed in his efforts to reduce the inversion. Twelve days later I was called to operate upon the patient. The inverted fundus, which was fully delivered from the vagina, was partially gangrenous. The fundus was amputated; recovery followed. The operation was performed on a kitchen table in a farmhouse.

CASE 3.—Mrs. C., aged thirty-five, para iii, was delivered by low forceps after a fairly easy labor of six hours duration. The placenta was expressed, but no great amount of force was employed. The inverted fundus appeared at the vulvar outlet immediately following the delivery of the placenta. There was little loss of blood and no pain. The patient went into profound shock but had rallied somewhat when I saw her an hour later. Efforts at reduction failed, due to the presence of a gripping cervix. The patient's pulse was running at about 160, but disappeared at every effort toward reduction. The fundus was pushed back into the vagina, a gauze pack applied and for four hours efforts were directed toward restoring the patient, but there was little or no improvement. Another effort was made to reduce the displacement and we again failed. I then proceeded to amputate the uterus. Because of the extreme shock I was able to complete the procedure without general or local anesthesia and without occasioning pain to the patient who was in a semiconscious condition. To those who advocate abdominal section in all such cases I would say it is my belief that this patient could not have withstood the added shock of the operation. As it was, the pulse regained its force immediately upon removal of the uterus and recovery was speedy and complete.

In perusing the literature on inversion of the uterus one is impressed with the diversity of opinion relative to its frequency of occurrence, its etiology, mechanism, prognosis, and treatment. In 1,932,164 labors collected from the literature, there were 17 inversions, or one to 113,068 labors. Zangemeister estimates 1 in 400,000, while Küster's estimate is 1 in 23,000. The extreme rarity of the occurrence is evidenced by the finding of but 76 cases reported in German literature in the past twenty-one years.

The inverted uterus has been tersely described as "upside down and inside out." Faulty technic in delivery is responsible for a large proportion of all recorded cases. Forceful expression of the placenta and traction on the cord are, of course, contributing factors in the production of inversion, but no amount of force in the effort to deliver

the placenta would invert a firmly contracted uterus, nor would the cord withstand sufficient traction to invaginate a uterus well contracted. Furthermore, these factors do not explain the occurrence of inversion in which the placenta has been delivered with no assistance. More than half the cases occur in primipara in whom fundal attachment of the placenta is more common than in multipara and the uterine contractions are more forceful. That fundal attachment of the placenta is not essential is evidenced by the occurrence of inversion in placenta previa. Moreover, a firmly contracted fundus may find its way through a dilated and relaxed lower uterine segment and cervix; hence, it is apparent that complete relaxation of the uterus is not essential to the development of inversion. Given a limited area of atony under direct pressure from above or traction from below and the contractions of the uterus may well participate in effecting a complete inversion. Reeve is quoted as saying that "the accident may occur independently of anything done or omitted."

Jones gives the following terse description of the mechanism of puerperal inversion: "After any portion of the uterus becomes indented to a considerable extent the rest of the organ seizes this invaginated portion as it would grasp a foreign body, and in attempting to expel it, turns itself inside out." This would seem to tell the story as well as it can be told. Doubtless spontaneous readjustment of a partial inversion not infrequently takes place and is seldom recognized where there is but an incupping of the fundus. Where there is general relaxation of the fundus the inverted portion is dragged in a downward direction. It is this traction in a downward direction that plays the chief rôle in forcing the inverted fundus into and through the relaxed cervical canal. The brutal force that is often applied to the uterus in endeavoring to deliver the placenta in the presence of uterine inertia and without causing inversion, adds emphasis to the factor of traction on the part of the incupping fundus. Probably one-third of all puerperal inversions arise spontaneously in the absence of traction on the cord or pressure from above. Eighteen of the 61 cases reported by Evans were spontaneous and without forcible expression or traction on the cord. Of the 437 postpartum inversions recorded by Thorn, 54 per cent were spontaneous and were not contributed to by traction on the cord or by forcible expression of the placenta. ✕

While inversion usually occurs within an hour after labor, it has been known to be delayed until the fifth day of the puerperium. It seems incredible that a diagnosis should be long delayed, but Peterson's case eluded recognition for twelve years and Reeve's for twenty-five years. As to time of recognition of the inversion Jones, in his analysis of 191 cases of acute inversion, found 19 recognized at the end of the second stage; 44 at the completion of the third stage; and 141 within twelve hours following delivery of the placenta. It is surprising, however, to



note the great number that have escaped recognition for one or more years. Instances of mistaken identity are recorded.

E. H. Smith (1897) writes of a midwife who pulled upon the inverted uterus for three-quarters of an hour and finally completed a manual hysterectomy with one tube and ovary thrown in for good measure. Incidentally, the patient survived. But the results were not so fortunate in a case attended by a midwife who mistook the inverted fundus for the head of a second child. She completed her task, but the patient died.

McCullagh says that half the cases show no immediate symptoms. With the placenta in situ or the cervix tightly constricting the protruding uterus, there will be little loss of blood. Shock may be present without hemorrhage and is variously ascribed to the sudden decrease in intraabdominal pressure, to compression of the ovaries (McCullagh), and to traction and stretching of peritoneal structures. With shock and hemorrhage averted there may be an interval of relative safety to be followed by gangrene of the uterus from strangulation and consequent sepsis.

The mortality is variously estimated at from 14 to 25 per cent. Here, again, we are at a loss to make any reliable statement, for the reason that many of these cases occur in the home, are often unrecognized, and are seldom recorded. Half the deaths occur in the hour following delivery and possibly nine deaths in ten occur within two hours of the completion of labor. Mason and Rucker, in an analysis of 63 cases, found no mortality in hospital cases where prompt and efficient treatment was available, this in comparison with a mortality of 12.5 per cent in the hands of the doctor in the home and of 26 per cent in the group delivered by midwives. Jasche estimates that about one-fourth of the deaths result from hemorrhage, one-fourth from shock, and the remaining half from sepsis. He believes that correct therapy could reduce the mortality to 3 or 4 per cent. In the 399 cases of acute puerperal inversion reported by Thorn, the mortality was 16 per cent. Approximately half the deaths were due to hemorrhage, nearly one-fourth to shock, and a trifle over one-fourth to sepsis. Two of the patients died of pulmonary embolism.

In considering the management of acute puerperal inversion we should bear in mind that a successful correction of the inversion at the expense of a life is not an obstetric triumph. In perusing the records of cases reported in the past twenty years, I am profoundly impressed by the appalling number of deaths following early or late upon a reduction of the displacement by taxis. Phillips records a mortality of 30 per cent following reposition in the presence of shock and hemorrhage, as contrasted with a mortality of only 5 per cent where no attempt at replacement was made prior to restoration of the patient from the effects of shock and hemorrhage. To attempt reposition in the presence of shock and profound anemia is to invite disaster. Unquestionably, the sheet anchor in the presence of shock and hemorrhage is blood transfusion. In studying case reports one is impressed by the number of lives saved by the simple process of checking hemorrhage by packs and

the transfusion of blood before resorting to any methods of replacement. Such precautionary measures will lower the mortality fully 50 per cent. The uterus has been replaced by taxis and the patient succumbs to shock and attending hemorrhage. Operative procedures, both vaginal and abdominal, have been employed in the presence of profound shock and the patient died. The uterus has been replaced by taxis or operation with delayed death from sepsis. In many instances the fatalities are unquestionably the result of ill-advised intervention in the presence of shock. A blanched patient is always a poor surgical risk and here, as in placenta previa, it is imperative first to control the loss of blood, second to combat shock, and with this accomplished, it is time enough to correct the inversion. In the absence of profound shock, great loss of blood and known sepsis, the uterus should be replaced and at the earliest possible time. Under such favorable conditions early replacement is seldom difficult. Delay of one or more hours may result in a tightening of the constricting cervix and defeat all attempts at replacement short of operation.

While hemorrhage is the cause of death in the greatest number of recorded cases, sepsis following replacement must be reckoned with. About one-third of all fatalities are ascribed to sepsis. Every inverted uterus is a potentially infected uterus, and in the presence of extreme depression and acute anemia it is not surprising that the morbidity and mortality from sepsis following replacement are so great. I am convinced that results would be bettered by a more general application of vaginal hysterectomy where there is good reason to fear sepsis. I would go one step further in advocating vaginal hysterectomy where vaginal replacement has failed, rather than to enter the abdomen under general anesthesia in the presence of profound shock. Better to sacrifice the uterus than the patient. I am aware of the splendid results recorded by Huntington, Kellogg, and Irving in which abdominal replacement was effected and in the presence of profound shock, but I affirm that such an undertaking would not be justified in the hands of less skillful operators. In a personal communication from Foster Kellogg he expresses preference for abdominal reposition in the presence of shock because of the readiness with which the uterus can be replaced with almost instantaneous disappearance of shock. He is of the opinion that more loss of blood and greater intensity of shock will result from efforts at vaginal replacement. I grant that his position is defensible under the favorable conditions of master surgery and modern hospital facilities. But, unhappily, such are not the usual conditions. The dictum in force when "Knighthood was in Flower" applies here with added force, "Choose your weapon according to your cunning."

## CANCER OF THE CERVIX COMPLICATING PREGNANCY

By JOHN A. McGLINN, M.D., PHILADELPHIA, PA.

THE literature on cancer of the cervix complicating pregnancy is most voluminous.

B. P. Watson, 1918, reviewed the subject and reported a most unusual case, the paper being discussed by H. M. Vineberg. This, and the recent report of E. Schumann, 1927, on the coexistence of cancer of the fundus of the uterus and pregnancy, are the only references to be found in the transactions of this Society. The importance of this subject and the paucity of our discussions justifies its consideration at this time. The subject is particularly important for the reason that the best and most modern treatment for cancer of the cervix may, in the light of more extended experiences, be contraindicated when pregnancy complicates the cancer.

It is difficult to estimate the statistical frequency of the association of cancer of the cervix and pregnancy. B. C. Hirst, 1923, reported a large series of cases showing an incidence of one case in every 12,484 pregnancies. Lately E. O. Gross reviewed practically the same number of pregnancies and found the incidence to be one in every 1,538. According to Mundell, Mussey reported an incidence of one in 437 pregnancies. Individual experiences differ just as widely. Herbert Spencer in the Lettsomian Lectures (*Proceedings of the Medical Society of London*, 1920), reports 10 cases. Hauch reports 4 cases, Gross 34, Korg 7, Bainbridge 2, myself 2, etc. Gross believes that the condition is five times more frequent than is supposed. This is most likely true if the cases of cancer which are recognized within a year after the termination of a pregnancy are included.

There is likely no causal relationship between pregnancy and cancer of the cervix in so far as their occurrence at the same time is concerned. As is to be expected the association is more likely to be found in multipara rather than primipara and in the late thirties rather than in the early twenties, these findings being dependent on the repeated traumatism to the cervix in multipara and the age incidence of cancer in general.

J. T. Williams in an exhaustive study of the literature was only able to find records of 8 cases of the association of cancer and pregnancy in primipara. Schilling in a study of 43 cases found the average number of pregnancies in each case to be 6.9. The two cases to be reported were both primiparas, one twenty-eight years old and the other thirty-one years old.

Goodal in a very important paper read before the Philadelphia County Medical Society several years ago, advocated the cleaning up of all erosions and infection of the cervix after labor as a preventive of infections in subsequent labors. If this advice was generally followed it would mean not only a lower incidence of infections but also a lower incidence of cancer in subsequent pregnancies. The broad application of the principles enunciated by Goodal would have a beneficent effect on the health of the child-bearing woman.

Gross in 1922 reported 34 cases of cancer of the cervix occurring within a year following pregnancy at term or abortion. He urges that a close follow-up should be kept for at least a year in all women over thirty who have had either a confinement or abortion. It is our practice to observe this rule in all such cases irrespective of the age and not to discharge an obstetric patient until the cervix is in a healthy condition. The general acceptance of this rule would result, not only in the early detection of some cases of cancer of the cervix, but would prevent the development of cancer in many.

There is to be found in the literature a decided difference of opinion as to the question of the antecedence of the cancer or the pregnancy. There may be room for an academic discussion of the pros and cons of this question but clinically there can be no difference of opinion. In many cases the cancer antedates the pregnancy, and in many cases the pregnancy antedates the cancer. This is demonstrated in my two cases. Cohnstein and Gross found that cancer antedated the pregnancy in 17 per cent of the cases they studied, whereas J. T. Williams, Blumreich, Keyes and others believed that in the majority of cases the woman had cancer before she became pregnant. As a matter of fact there is no reason why a woman with early cancer of the cervix should not become pregnant nor is there any known reason why the pregnant woman should not develop cancer.

The same difference of opinion is found in regard to the question of the influence of the pregnancy on the cancer. The opinions expressed as a rule depend on what the author has observed in his individual case. If there has been rapid spread of the disease he usually argues that pregnancy has been the cause of the rapid increase. If, on the other hand, there has been retardation of the growth, specious arguments are brought forward to prove that pregnancy has a deterrent effect on the cancer. Undoubtedly many observers have noted a marked rapidity of cancer growth associated with pregnancy, such as the classical examples of Zweifel and Simpson. On the other hand, many observers, notably Weibel, Wolf, Meyer, etc., have observed a retardation of the growth, and have advanced theories in support of this observation. We recognize, however, that cancers vary greatly in their malignancy; so that, unless it is known what type of cancer we are dealing with in each individual case, it is impossible to draw any accurate conclusion on this question.

Much has been written on the symptomatology and diagnosis of the association of pregnancy and cancer of the cervix. Certain facts stand out: Bleeding is the leading symptom and a careful examination for the cause of all bleedings in pregnancy discloses the true condition. The mistake is made of considering all bleedings in the early months of pregnancy as due to threatened abortion and refraining from making an examination. In the later months of pregnancy placenta previa or accidental hemorrhage is suspected and again we fear the danger of an examination. We have become obsessed with the fear of mak-

ing a vaginal examination in pregnancy. The dangers of vaginal examination are grossly exaggerated. If we can teach how to learn something from a rectal examination, we can teach how to make a vaginal examination without endangering the patient. Unless all cases of bleeding during pregnancy and early puerperium are fully and competently examined, many cases of early cancer will be missed. There is no mystery in making a diagnosis, it is simply a case of looking for it.

I have observed two cases, one in early pregnancy properly diagnosed, and one in late pregnancy, mistakenly diagnosed.

CASE 1 was in a primipara thirty-one years old, married two years. Five months prior (June) to consulting us, she had a slight discharge and consulted a physician on account of the discharge and sterility. He found a slight abrasion of the cervix which was treated locally. She menstruated in June, July, and August. In September slight bleeding but not a regular period, no bleeding in October. Early in November she started to spot. Examination on November twenty-first revealed a uterus the size of a three months' pregnancy with a punched-out ulcer one-half inch in diameter on the posterior lip of the cervix. Dark-field examination and Wassermann negative for syphilis. Excision of the ulcer followed by extensive cauterization of the operative area was the next step in the study of the case. The pathologic diagnosis was cancer of the cervix. This was a very early case, in fact, the earliest case of cancer of the cervix I have ever seen. Complete hysterectomy was advised and refused. Radium was then suggested but the patient refused to have anything done which would jeopardize the life of the child in any way. This attitude was dependent entirely on an inordinate desire for a child. She finally consented to the use of radium, and was given 2400 mg., hours by capsule and needles into the cervix. This was quickly followed by a most remarkable disappearance of all local evidence of the disease. The uterus, however, did not enlarge and four weeks after the application of the radium she aborted a three months' fetus.

The laboratory report follows: Specimen is a male fetus, placenta and membranes. Fetus is slightly macerated: measures 17 cm. from crown to sole, 10 cm. from crown to rump, weighs 85 gm. Cord is 16 cm. long by 0.6 cm. thick. Placenta is 8 cm. in diameter by 2 cm. thick and is complete. Membranes seem slightly thickened. Placental tissue is pinkish grey in color, mottled along the border by brownish-red. Sections of placental tissue reveal slight cellular degeneration with a scattered mixed leucocytic exudate throughout. Otherwise negative. Blood vessels of cord also show this infiltrate in all layers. There is no definite thrombotic occlusion to be expected from the macroscopic appearances, but interference with vascularity has undoubtedly produced death of fetus.

Patient was discharged from the hospital in good condition with no evidence of the disease. She was examined at regular intervals and remained symptom free until the following August, nine months after the radium and eight months subsequent to the abortion. She then complained of pain in the pelvis and examination showed a small mass in the left broad ligament. Section revealed multiple metastases in the pelvis. She later developed acute mania and had to be removed to a psychopathic hospital, where she died.

This case presents some interesting phases. First, the cancer undoubtedly antedated the pregnancy in a fairly young primipara. Secondly, cauterization and radium apparently cured the cancer of the

cervix, yet pelvic metastases occurred later without any return of the local condition. Thirdly, radium, by its action on the circulation of the cord and placenta caused the death of the fetus.

CASE 2.—Primipara, twenty-eight years old. Late in pregnancy she developed severe bleeding which was diagnosed as due to placenta previa. A living child was delivered by cesarean section. She was still having vaginal bleeding when she was discharged from the hospital. I saw her soon after this and found an advanced inoperable cancer of the cervix and vagina. We gave her an application of 3600 mg. hours of radium with excellent local results and referred her to Dr. G. E. Pfahler for deep x-ray treatments. Ten months later she was in good general health but with a pelvis blocked by cancer. She is still living, one and a half years after being treated.

The interesting phase in this case is the mistaken diagnosis of placenta previa. This case, from the extent of the disease when we first saw her, must have had symptoms long before she was operated upon. Had examinations been made, the disease might have been recognized in time to have cured her cancer.

The prognosis for the mother, no matter the stage of pregnancy, is bad but not altogether hopeless. A number of reports of cures after hysterectomy, radium and cautery amputation of the cervix, are to be found in the literature. None are more interesting than those reported by Herbert Spencer. Three of his cases remained well after nineteen, twenty-two, and twenty-five years. The last of these had a child subsequently to the cautery amputation, delivered by cesarean section, who served as a soldier in the Great War.

The prognosis for the child depends on the stage of pregnancy and the method of treatment adopted. Obviously the child's chances are best when the cancer develops late in pregnancy and when delivery is made by cesarean section without any prior treatment of the cancer. Per contra, the prognosis is worse when the cancer occurs early in pregnancy and the uterus is removed. The effect of treatment on prognosis of the child will be discussed later.

Next to the early recognition of the disease, the question of treatment is most important. All authorities are in accord that abortion has no place in the treatment of this complication. There is also general accord that a case treated with radium should not be allowed to go into labor but should be delivered by cesarean section. There is not the same general accord in those cases apparently cured by cautery amputation, though I believe the majority of authorities would not permit a cervix, once the seat of cancer, ever to be traumatized by a subsequent labor. While cases have been safely delivered by normal labor, cesarean section is undoubtedly the best method of delivery.

I take it there would be general agreement in favor of complete hysterectomy in the first three months of pregnancy where the cancer is limited entirely to the cervix. There will likely be little objection to the statement that in the late months of pregnancy the case should

be terminated by cesarean section with immediate hysterectomy or subsequent treatment with radium and x-ray, the choice of immediate hysterectomy or subsequent radiation depending on the stage and character of the cancer.

The prime question to answer is what shall be the treatment in the cases with the cancer too far advanced for hysterectomy and the pregnancy not far enough advanced for delivery of a viable child by section. It is now generally conceded in this country, in all borderline cases of cancer of the cervix, radium application is the method of choice. In many clinics radium has supplanted operation in all cases of cancer of the cervix. When we come to consider radium in cancer of the cervix associated with pregnancy, however, we face a new and difficult problem to solve. We have to consider not only the effect of radium on the child, but also the effect of the treatment on the cancer. While some cases have been treated with radium and gone to term to be delivered of a child, in many of the cases, as in my own, the fetus has been promptly killed and abortion has resulted. Abortion is a dangerous complication even after radiation. Channels are opened up for the spread of the disease before the radium has had a chance to fully protect the woman and metastases kill as in the case just reported. On the other hand, radium may cure the cancer and if the fetus does not die, the effects on the child may be most deleterious. Much has been written on the effects of radium on the fetus in utero. The conclusions have been based on the results of animal experimentation and clinical observations in the human. Goldstein (*AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY* 16: 747) has reviewed the experimental literature and compiled the bibliography. Murphy (*Surgery, Gynecology and Obstetrics*, August, 1928) reviews the clinical as well as the experimental literature and attaches a complete bibliography. Both of these splendid pieces of work were done under the direction of Dr. C. C. Norris.

#### CONCLUSIONS

"Irradiation of pregnant animals or human beings is a procedure extremely dangerous to the health of the offspring concerned (61.3 per cent defective), and in the case of human beings ought not be undertaken unless such existing pregnancies are to be terminated artificially prior to the period of viability of the child.

"As yet, it cannot definitely be stated that preconception maternal pelvic radium application or x-ray irradiation is or is not prejudicial to the health of subsequent child."

In drawing conclusions from the literature care should be taken to separate the cases radiated prior to pregnancy and those radiated during pregnancy. While there may be some doubt as to the effect of preconception radiation on subsequent children, there can be little

doubt as to the serious defects which may develop in the fetus as the result of radiation following conception. While our knowledge is not sufficient at present to draw definite conclusions, it is enough to cause us to elect to do either a complete hysterectomy or a cautery amputation of the cervix rather than to use radium when pregnancy complicates the cancer.

The effects on the child both in pre- and postconception radiation is about the most important question to be solved at the present time. It is urged that every one should carefully record their experiences so that conclusions based on a study of a large series of cases can be drawn.

1900 RITTENHOUSE SQUARE.

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## A STUDY OF TWO HUNDRED AUTOPSIES MADE ON SYPHILITIC FETUSES\*

By J. R. McCORD, M.D., ATLANTA, GA.

*(From the Department of Obstetrics, Emory University School of Medicine)*

THE study of syphilis and pregnancy in the colored race, in the South, is an economic as well as a scientific obligation. In a former study published several years ago I found that, of the stillbirths and early neonatal deaths in our clinic, 45 per cent had syphilis and 12 per cent more probably had syphilis. The incidence of syphilis in this present study is 41 per cent, with a probable incidence of an additional 8 per cent. The smaller percentage in the present study is perhaps due to the fact that more early abortions were studied in this series. The organisms of syphilis were found in 61 babies. The mothers of 3 of these babies had attended the antisyphilitic prenatal clinic; 2 of these mothers had one arsenical treatment, and the other had two treatments. Every baby was examined under the roentgen ray for evidences of syphilis in the long bones. The bones were positive in 83 babies, or 41 per cent. The mothers of only 10 of these babies had attended the antisyphilitic prenatal clinic. Not one of these mothers received more than three treatments.

### THE DIAGNOSIS OF SYPHILIS

A positive diagnosis of syphilis was made upon the finding of one or both of the following: the demonstration of the organisms of syphilis in the stained tissues, and the characteristic lesions of the long bones as revealed by the roentgen ray.

A probable diagnosis of syphilis was made when the maternal blood Wassermann reaction was strongly positive and the histologic changes in the mature placenta were plainly positive.

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\*Read by invitation.



## PREMATURITY

One hundred and thirty-nine, or 69.5 per cent, of the babies were premature. Of these premature babies, 52 per cent had syphilis. Seven other premature infants probably had syphilis.

Intrauterine age was roughly estimated by the weight which was, in most cases, taken at birth. The accompanying table shows the weights, the number of fetuses in which the bone changes were positive, the organisms of syphilis found, or both. The smallest fetus in which the organisms of syphilis were found weighed one hundred grams; they were found in two that weighed two hundred grams, and in one that weighed three hundred and twenty grams.

<i>Fetus</i>	<i>Grams</i>
5	100- 500
6	500-1000
13	1000-1500
19	1500-2000
23	2000-2500
8	2500-3000
1	3000-3500

Fifty-seven babies were born at or about term; of these, 14 were syphilitic and 3 more probably had syphilis. There were 161 stillbirths; 39, or 19.5 per cent, were born alive.

## HISTOLOGY

I have been able to find but little histologic work, either normal or abnormal, on the newborn. Maceration causes most of the tissues of value to be unfit for study. When perivascular infiltrations of small round cells have been found, the baby has been syphilitic in most cases; the absence of such lesions, however, does not exclude syphilis. Thickening of the walls of the blood vessels and an increase of connective tissue were found almost as often in the cases that did not have syphilis, as in those that had the disease. A gumma, recognizable as such, was not found in the entire series. This includes the histologic studies of the placentas. A better trained pathologist would probably have obtained a great deal more information from this work than I have, but I feel that it is safe to make a positive diagnosis of fetal syphilis from the presence of the organisms in the tissues and the frank long bone lesions. When perivascular infiltrations of small round cells and marked connective tissue proliferation are seen, one or both of these positive diagnostic evidences can be demonstrated. The converse of this statement is not true; that is, one or both of these positive diagnostic evidences can be demonstrated without the presence of perivascular infiltrations of small round cells or marked connective

tissue proliferation. Complete histologic studies were made on 61 cases, but the results were so uncertain and so variable they will not be reported at this time.

#### LONG BONE CHANGES

The long bone changes were positive in 83 of the 200 cases studied, a percentage of 41. The bones were positive and the organisms of syphilis were not found in 17 babies. I can explain this discrepancy only by the belief that in certain cases the organisms of syphilis do not take the silver stain. The bones were negative twice where the organisms were present. The bones were positive in 7 cases where no silver staining was done. The bones were positive and the placentas positive in 48 cases; the bones were positive and the placentas premature positive in 10 cases.

#### MATERNAL WASSERMANN REACTIONS

Negative reactions were obtained 108 times; 82 were positive and there were 10 mothers on whom the test was not made. Forty-three per cent of the reactions were positive. The blood Wassermanns on the mothers and the long bone lesions in the babies were both positive 55 times. The bones in the babies were positive and the maternal Wassermann tests were negative 21 times. The organisms of syphilis were found in 15 babies whose mothers had negative Wassermanns, and were found in 43 babies whose mothers had positive Wassermanns. The maternal and cord Wassermanns were positive in 5 cases. (Because of death and maceration relatively few specimens of cord blood could be obtained.) The bone lesions of syphilis were demonstrated in 6 babies whose mothers had no blood Wassermann tests. The maternal Wassermanns were negative in 5 cases in which the cord Wassermanns were positive.

#### CORD WASSERMANN

Only 88 cord Wassermanns were done, yet 25 per cent of them were positive. The cord Wassermann reactions were negative on 8 babies who had syphilis, and positive on 20 babies with syphilis. The reactions were negative in 4 cases with probable syphilis. The organisms of syphilis were found in 37 babies on whom cord Wassermanns were not done. The long bone changes were positive in 56 babies where the cord Wassermanns were not done. Evidences of syphilis were seen in the bones of 5 babies whose cord Wassermanns were negative. Both cord Wassermanns and long bone changes were positive in 20 cases.

#### THE ORGANISMS OF SYPHILIS

The original Levaditi method of staining the organisms was used. The following tissues were routinely examined: brain, eye, thymus, lungs, kidneys, suprarenals, spleen, heart, liver, aorta, cord, uterus,

fallopian tubes, skin and, in some cases, the testicles. The tissues from 189 babies were stained. The organisms of syphilis were found in 61 cases, or 32.3 per cent. The stain was unfit for study in 11 cases.

The organisms of syphilis are a puzzle to me. Why should they be found in the placenta and not in the baby? Why should some autopsies reveal literally millions of them, and others, with positive maternal and cord Wassermanns, syphilitic bone changes and positive placentas, after prolonged search reveal none? Sometimes the organisms are long, then short, a few spirals, many spirals; some are thin, others are thick. It is probable that the thicker the connective tissue in which the organisms are embedded, the longer and thicker they are apt to be.

It would seem that the smallest organisms have been most frequently seen in macerated tissues. Fragmented organisms are often seen in macerated tissues; they appear distributed in showers. The fact that the organisms were found in 15 babies whose mothers had negative blood Wassermanns, will bear repeating.

#### HISTOLOGY OF THE PLACENTA

The histologic diagnosis of syphilis in a placenta at or near term is, as a rule, an easy diagnosis to make. I agree with Holland that the histologic diagnosis of syphilis in a premature placenta is exceedingly difficult. The more premature the placenta, the more difficult it is to express an opinion.

Thirty-nine per cent of the 115 placentas examined were diagnosed as positive for syphilis without comment. The diagnosis of premature positive was made on 26. Some additional data in connection with the premature placentas is as follows:

Premature positive placentas		26
Maternal Wassermann	{ Negative	9
	{ Positive	17
X-Ray Baby	{ Negative	16
	{ Positive	10

No placenta had a negative finding where spirochetes were found in the baby. When the organisms of syphilis were found in the baby, the premature placentas of doubtful histology were classified as positive. The placentas were positive and the maternal Wassermanns negative 9 times, and premature positive with negative maternal Wassermanns 7 times. The placentas were negative and the maternal Wassermanns positive 9 times. The placentas and maternal Wassermanns were both positive 37 times. The premature positive placentas and positive maternal Wassermanns agreed in 16 instances. There were 37 positive placentas where the organisms were found in the baby. The spirochetes were found in 17 babies where the placentas

were not studied. The organisms of syphilis were found in 2 placentas but prolonged search failed to show them in either baby. No placentas were negative with positive bone changes in the baby. If the placenta is mature and the histologic changes are characteristic of syphilis, there are, in almost every instance, definite evidences of bone destruction in the baby, and the organisms of syphilis can be found in the majority of cases. A syphilitic placenta with no evidences of the disease in a live baby is an indication for prolonged study and constant observation. Patchy areas that appear syphilitic should only arouse suspicion.

There were 32 cases in which the placentas, bone changes, and maternal Wassermanns were all positive, and in whom spirochetes were found in the tissues.

#### SOME CAUSES OF DEATH

As a matter of interest, the accompanying list gives the conditions named as having caused the deaths of some of the babies:

32	Prematurity
18	Undetermined
18	Toxemia of mother
10	Intrauterine asphyxia
6	Brain hemorrhage
4	Pneumonia
1	Atelectasis
3	Premature separation of placenta
2	Prolapse of cord
1	Pyelitis of mother
1	Prematurity of twins
1	Prematurity (one of twins)
1	Suffocation

The following conclusions may be considered axiomatic:

1. Syphilis is only transmitted to the baby by way of the placenta.
2. The lesions of the long bones as demonstrated by the roentgen ray are pathognomonic of fetal syphilis.
3. The organisms of syphilis fail to stain in a certain number of cases—probably in as many as 12 to 15 per cent.
4. A mature placenta with the histology of syphilis is rarely found without other positive evidences.
5. Even moderate antisymphilitic treatment during pregnancy will save a majority of babies.
6. Mild arsenical and mercurial treatments have no injurious effects upon pregnant women.

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## Original Communications

### OVARIAN HYPOFUNCTION, HABITUALLY DELAYED AND SCANTY MENSTRUATION, IN RELATION TO STERILITY AND LOWERED FERTILITY

A CLINICAL AND STATISTICAL STUDY\*

BY I. C. RUBIN, M.D., F.A.C.S., NEW YORK CITY  
(Associate Gynecologist, Mt. Sinai Hospital)

HABITUAL delay of the menses has recently come to be recognized as a symptom of menstrual abnormality for which patients seek relief more frequently than heretofore. Although prolonged absence of menstruation has been generally regarded as a symptom of poor health, it did not cause women to seek medical advice as often as for menorrhagia or metrorrhagia. As long as the menses maintained some periodicity, patients did not mind their infrequent occurrence. Girls of school and college age even welcomed this tardiness because it enabled them to indulge more fully in sports, dancing, etc. They were, however, more apt to be disturbed by associated symptoms, such as increasing obesity, lassitude, mental torpor, headache—occasionally by hot flushes.

Married women whose menses are delayed or diminished find that they are not as susceptible to conception as those who menstruate normally. After several years of married life they regard themselves as sterile. Sterility then assumes major importance, the delayed periods being of secondary interest.

\*From the Gynecological Service of Mt. Sinai Hospital and my private practice.  
Read by title at the Fifty-fourth Annual Meeting of the American Gynecological Society, Old Point Comfort, Va., May 20-22, 1929.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

GENERAL CONSIDERATIONS BEARING UPON THE RELATIONSHIP BETWEEN  
 OVARIAN FUNCTION AND MENSTRUATION. DEPENDENCE OF  
 MENSTRUATION UPON OVARIAN FUNCTION

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The most significant recent contribution bearing upon the relationship between ovulation and menstruation is to be found in Corner's work in mature females of the *macacus-rhesus* family.<sup>1</sup> He was able to show that in this monkey family menstruation frequently occurs without ovulation. However, when ovulation occurs it seems to take place at a definite time, about twelve or fourteen days before the onset of the menstruation. Menstruation without ovulation is not preceded by the so-called premenstrual changes of the endometrium which occur only after the formation of the corpus luteum. He found evidence of ovulation in 7 out of 27 cycles of menstruation where the data were obtained and known either through autopsy or exploration.

Whether or not we may conclude a similar relationship between menstruation and ovulation in the human species, one fact appears to be firmly established, namely, that the ovarian changes are primary and the uterine changes secondary. If Corner's observations in the monkey should hold for the human species, it would enable us to explain why any woman who has conceived once or twice may not readily conceive again, all other factors of course being excluded. It would also explain why some women are susceptible at some seasons of the year or at certain times, whereas at other times and for varying intervals they remain infertile. It would further indicate the possibility that the endometrium does not regularly undergo the typical fully developed pregravid changes with each menstrual cycle that under normal physiologic circumstances prepare the uterus for ovular nidation.

It is not illogical to assume that the menstruation which is not preceded by ovulation is also associated with an atypical, ill-developed uterine mucosa, and that the type of menses in such instance would in all probability be altered. This is of course hypothetical and observations in human material "in the light of the new facts discovered in a related species" are much to be desired, according to Corner.

In the light of Corner's findings and of clinical experience, we cannot escape the conclusion that the average woman who menstruates regularly is not capable of being impregnated each month; that therefore, her chances for conception are perhaps thus reduced to once in several menstrual cycles. Consequently, women who menstruate less frequently than once in four weeks, all other factors being equal, may be expected to have proportionately less available ripe or fertile ova than those who menstruate every twenty-eight days.

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NOTE: For lack of space certain parts of this paper have been omitted. The paper will be published in full in the current volume of the Society's Transactions (1929) as well as in the author's reprints.

WHAT IS THE UNDERLYING HISTOPATHOLOGY OF THE OVARIES IN CASES OF  
DELAYED MENSES?

Data with respect to the anatomic condition of the ovaries in cases of scanty menstruation are unfortunately not available. The same holds true for habitually delayed menstruation.

Unless there is present some abnormality, such as fibroids, ovarian cysts, etc., indicating the need of a laparotomy, these patients are seldom operated upon, so that observations upon the ovaries are rare and perhaps unrecorded. Inasmuch as ovarian removal is certainly not warranted the opportunity for histologic examination of the ovaries is not at hand. C. Jeff Miller in a critical review of the treatment of sterility by roentgen ray therapy<sup>2</sup> mentions a case of Heimann's which was subjected to x-ray irradiation. Heimann studied the ovary, which was removed later during laparotomy for other reasons, and found both macroscopically and microscopically that its variations from normal were so slight as to be negligible. This incidentally proved the harmlessness of fractional x-ray treatment for amenorrhea.

I have had an opportunity of examining the ovaries in two cases of habitual amenorrhea. In one patient macroscopic inspection as well as microscopic study of the ovaries was possible. This patient, twenty-two years old, had been married four years, having given birth to one child ten months previously. Her menses began at the age of thirteen, and were always delayed, one, two or three months; bleeding often lasted eight days. Examination showed the uterus to be globular, in anterior position, not enlarged; the cervix was small and the adnexa were not palpable. On February 8, 1922, on account of a seizure of severe lower abdominal cramps, spotting after a delayed period, and three attacks of syncope, a laparotomy was performed. The pelvic peritoneal cavity contained a few ounces of dark blood. The tubes oozed blood. There was no evidence of an ectopic pregnancy. *The ovaries were found to be microcystic*, enlarged at least twice the normal size. They were partially resected; a portion  $4\frac{1}{4}$  cm. by 2 cm. by  $1\frac{1}{4}$  cm. from the right ovary and one  $5\frac{1}{4}$  cm. by  $2\frac{1}{2}$  cm. by 2 cm. from the left ovary were removed. The ovarian surface was absolutely smooth and pale. Here and there small cysts the size of a pea shimmered through the surface. (See illustrations.)

Microscopic examination showed a conspicuous absence of a fresh corpus luteum or of recent corpora lutea and of maturing follicles. One corpus luteum in marked regression (corpus albicans) was seen. Two smaller hyalinized bodies were present in the same ovary. There were relatively few primordial ova and even less primordial follicles. A few follicle cysts, one of which showed a well-marked theca lutein lining, were seen. The tunica albuginea was thickened and hyaline. The other ovary showed larger follicle cysts, few primordial ova and follicles, and no corpora lutea or maturing follicles.



In the other case the ovaries were inspected at the laparotomy operation for cesarean delivery. This was a woman forty years old whose menses began at the age of fourteen and were always irregular, being delayed three, four or five months. Between the ages of eighteen and nineteen amenorrhea which lasted almost two years had its beginning.

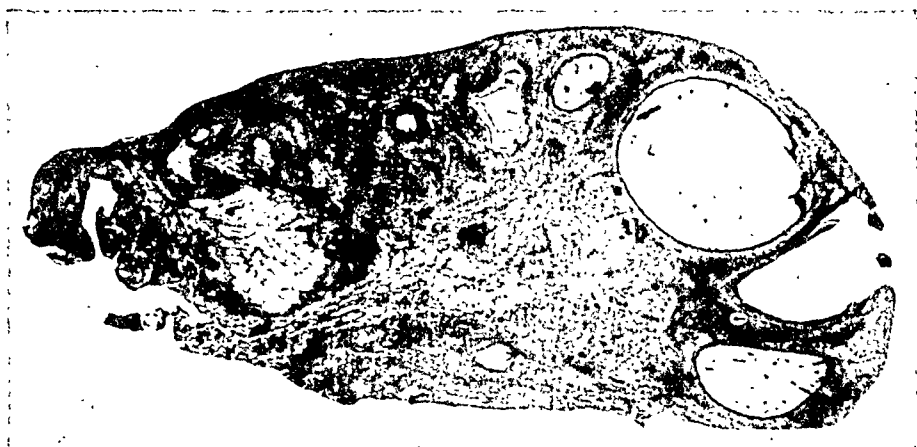


Fig. 1-A.



Fig. 1-B.

Fig. 1-A. and B.—Sagittal and transverse sections of right ovary. A corpus albicans is present.

The ovaries were flattened out, elongated, and enlarged. The surface was smooth and here and there were bluish-tinged cysts not projecting through the cortex. The appearance, however, was not unlike that of ovaries seen in pregnancy at term. The ovaries were not removed.

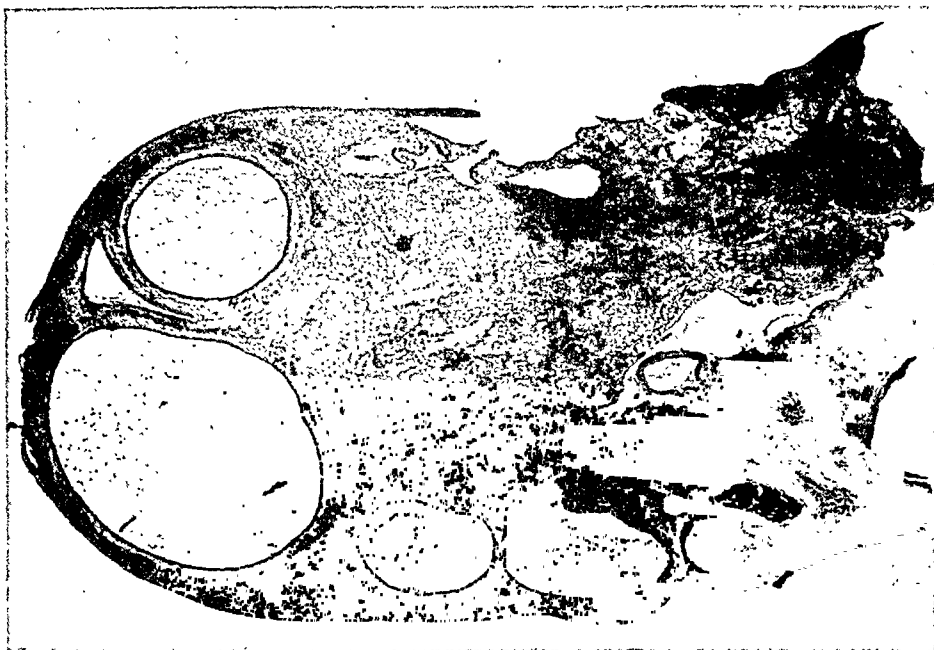


Fig. 2-A.



Fig. 2-B.

Fig. 2-A and B.—Left ovary. Follicle cysts are more numerous than in the right ovary. Theca lutein proliferation in centrally located follicle. No corpus luteum in any stage of development or regression.

This patient had been married nine and one-half years before she became pregnant. She had been treated for sterility with various gland extracts but had not been subjected to x-ray treatment.

\* \* \* \* \*

Owing to the scarcity in anatomic material, we are forced to assume what the changes in the ovaries may be. However, the law of cause and effect operates so uniformly with respect to primary changes in the ovary and secondary resultant changes in the uterus that we may get an idea of the former by observing the latter.

In cases of anticipated menses and menses of the twenty-one- or twenty-two-day type Schroeder found a definite acceleration and shortening of the various phases of the endometrial cycle. The ripe ovum dies prematurely; the granulosa gland as well as the endometrium degenerates prematurely, terminating in menstruation within three weeks instead of four. In the few cases of prolonged menstrual cycle which Schroeder examined, he found that the time of ovulation was postponed with a corresponding shortening of the corpus luteum and secretory phases, i.e., of the phase of the ripe ovum. There was at the same time a lengthening of the duration and onset of the follicle ripening phase. These observations, Schroeder remarks, cannot be relied upon, however, as they have not been substantiated by a sufficient number of well-controlled cases.

If there are no data with regard to the anatomic (morphologic) changes in the ovaries, there are fortunately some data as to the status of the endometrium in these cases of amenorrhea observed during the World War.<sup>4</sup> Histologic examinations of the uterine mucosa in women suffering from amenorrhea in the postwar period were made by J. Novak. He found that malnutrition causes definite changes in the genitals, varying from mild to more advanced types. In some patients there was a cyclical change of the uterine mucosa to a certain extent, without reaching the full premenstrual development. In other cases there was no evidence of any cyclical change, but at the same time, however, no marked regression. Here the mucosa was found to be in the resting stage. In a third group of patients it was more or less atrophic. That these different mucosal pictures indicate parallel ovarian changes must be assumed. In the majority of these cases there was restoration of function. In some, menstruation failed to return. These changes were also found associated with diabetes, severe gastrointestinal diseases, and other conditions which caused undernutrition.

Persistent corpus luteum has been found in some cases of temporary amenorrhea; in a few cases a polymicrocystic condition. The latter is more commonly found in instances of functional metrorrhagia. Not a small proportion of the patients with delayed menses gave a history of frequent uterine bleeding.

Another way in which some idea of ovarian function and hypofunction can be obtained is offered by investigating the female sex hormone content of the blood or urine. Frank and Goldberger have examined some 50 patients with amenorrhea. They found three types of conditions:

1. A regular subthreshold blood cycle.
2. No blood cycle.
3. An irregular, occasional blood cycle. They are therefore inclined to base their prognoses on these findings.<sup>5</sup>

Finally, still another method may be found in the behavior of tubal peristalsis during uterotubal insufflation. The effect upon the tubal musculature of ovarian hormone has been demonstrated to vary with the phase of the menstrual ovarian cycle.<sup>6</sup>

#### OVULAR AND FOLLICULAR CONTENT OF THE OVARIES AND FACTORS THAT INFLUENCE FOLLICLE DESTRUCTION

\* \* \* \* \*

Destruction of follicles apparently goes on under normal conditions from birth to puberty. The speed of destruction probably depends upon the general constitution of the individual, her environment, hygienic conditions, mental and physical exertion and strain, especially of school studies, and the psychic predisposition. Intercurrent diseases with their complications, malnutrition, avitaminosis, low caloric diets (as witnessed in the war zones abroad) as other factors. Toxic states induce more rapid destruction of follicles, impairing the vitality of those that would under normal circumstances ripen into the typical graafian follicle and eventually into corpora lutea.

Acute infectious diseases, such as typhoid, typhus, influenza, and erysipelas, may initiate an amenorrhea of shorter or longer duration. Lues and malaria through the ravages on nutrition may produce the same result. Mumps is a well-known cause. Pulmonary tuberculosis is frequently associated with amenorrhea. In this condition it is said to be a benign symptom. It is present frequently in genital tuberculosis and may be the only sign suggestive of this infection.

In the group of depressed menstrual disorders discussed at present we exclude tumors of the ovaries and acute and chronic inflammation, for in the vast majority of the cases under consideration the ovaries are free and not the seat of tumors. Gynatresias, both congenital and acquired, are also excluded.

#### RELATIONSHIP BETWEEN OVARIAN DISTURBANCES, MENSTRUAL DISORDERS, AND OTHER ENDOCRINOPATHIC CONDITIONS

An important group into which some of our cases fell is associated with endocrine disturbances. The ovaries are secondarily or simultaneously affected. The hypophyseal disorders are most frequently ac-

accompanied by menstrual disturbances. The worst cases are those of dystrophia adiposogenitalis where the amenorrhea is combined with genital atrophy. In acromegaly the menses can be restored when the tumor is removed. In hypophyseal cachexia (Simmonds' disease) the genital atrophy can be very pronounced. The same is true of multiple endocrine sclerosis in which the hypophysis, thyroid, adrenals, and gonads are severely affected.

The thyroid, thymus, and pancreas influence menstruation to a lesser degree. In Basedow's disease the patient may complain of amenorrhea but it is not the general rule. With the exception of the hypophysis the adrenal gland affects menses to a more marked degree than these glands. Patients with Addison's disease may lose their menses or they may retain them and even conceive.

In an analysis of 167 personal cases\* it was found that 55 cases, or 33 per cent, showed some aberration in the secondary sex characters, showing a masculine distribution of the pubic and abdominal hair with or without general hirsutism. In 54 cases a marked gain in weight was noted. Routine basal metabolism determinations were unfortunately not carried out. In 25 cases thus examined, 10 showed a low basal metabolic rate which varied from minus 11 to minus 32, the average reduction being minus 21. There was no definite relationship between the menstrual delay and the basal metabolic rate. In 3 of the patients the basal metabolic rate was sufficiently increased to indicate hyperthyroidism. In 12 patients the basal metabolic rate was within normal limits. One of the patients showing the lowest basal metabolic rate, i.e., minus 32, had other stigmas of polyglandular disturbance.

It will be recalled in this connection that Litzenberg<sup>8</sup> found a low metabolic rate in 50 per cent of sterile women, and of those treated with thyroid extract one-third conceived. "One woman of the group became pregnant three times under treatment, bringing the percentage of conception to forty." In a second report Litzenberg speaks of a sterility of 56 per cent in his cases. Forty-four per cent of the 137 women with a low rate had menstrual difficulties: amenorrhea, irregularity, menorrhagia, dysmenorrhea, and scanty flow. Litzenberg<sup>9</sup> concludes from his studies that "restoring the metabolic rate to normal by thyroid medication (and hygienic measures) in some cases improves menstruation, permits conception and prevents interruption of pregnancy."

Only one-third of my cases showed symptoms of endocrine disturbance, which were for the most part mild. Of the 76 cases of mild oligomenorrhea (six to eight weeks' delay) the following data were noted in 44: 24 had gained appreciably in weight; 20 showed male hair distribution.

\*This analysis was kindly made for me by Dr. Seymour Wimpfheimer, former resident gynecologist of Mt. Sinai Hospital, to whom I am deeply obliged.

In the group of moderate oligomenorrhea (three to six months) consisting of 35 cases, changes were noted in 25. In 13 a gain in weight was the predominant symptom, and in 12 there was some form of hirsutism.

In the group of severe oligomenorrhea (seven months to a year or more), of which there were 5 cases, 3 had gained in weight and 2 showed some type of hirsutism. Of the mild hypooligomenorrhea there were 5 cases, but only 2 showed changes: one a gain in weight and one with hirsuties. In the group of moderate hypooligomenorrhea there were 7 cases; 4 showed change: one, a gain in weight; in the other 3 some form of hirsutism.

Of 16 patients whose periods were regular until marriage, 8 showed some changes; 5 gain in weight; 4 some type of hirsutism. Of the 20 patients with disturbed regularity in menses due to some physical or mental accident, 10 showed changes: 9 a gain in weight and one, signs of virilism. Finally, of 3 patients with complete amenorrhea, all showed a well-marked hirsutism and one had taken on excessive weight. It seems, therefore, that the tendency to gain in weight is greater in those patients with longer periods of amenorrhea. Hirsutism appears to be a striking finding in these cases of delayed and irregular periods.

Marked psychic disturbances, such as sudden fright, great anxiety, fear of a pregnancy, or fear of not becoming pregnant can inhibit the onset of the menses. During the war, J. Novak says, an explosion in a munition factory caused an endemic outbreak of amenorrhea among the factory workers. Psychogenic amenorrhea is not an infrequent condition in time of peace.

\* \* \* \* \*

#### THE EFFECT OF MARRIAGE ON MENSTRUATION

In 16 patients the menstrual disturbance began after marriage. In 18 patients with a history of prenuptial menstrual delay, the disturbance became more marked, the periods of delay becoming longer. Eighty-eight patients, or 53 per cent, showed no change in the menstrual cycle. In 10 patients, or 6 per cent, some improvement was noted. There were no patients who became absolutely regular after marriage. On the other hand it is difficult to determine from this study which patient is rendered worse by marriage, as the cases fell into all the above groups with varying periods of amenorrhea. Spontaneous improvement occurred in a few cases.

The associated symptoms of amenorrhea will not be discussed here. As a rule if there are underlying causes they will manifest themselves in disturbances referable to the organs and systems of organs. We are here concerned rather with a more important symptom of hypoovarian disturbances, namely, sterility. Data with regard to the local genitals, the secondary sex characters, and the general constitution were noted.

There were no systematic measurements of the length of the extremities, of the epiphyseal union, of the sella turcica. There were no systematic blood calcium studies or blood pressure determinations, basal metabolism readings, or full blood examinations. The question of deprivation symptoms, of the libido, and other related matters of the genital sphere have also not been dwelt upon. These have been begun more recently and will undoubtedly prove of interest and value in the future.

\* \* \* \* \*

#### STATISTICAL ANALYSIS

The symptom complex of ovarian hypofunction and scanty and delayed menses is associated with sterility or lowered fertility.

Since 1915 when Van der Velde began to irradiate the ovaries in cases of oligomenorrhea and amenorrhea, a large number of publications have appeared dealing with this subject.

That pregnancy followed this treatment was noted by Flatau and Thaler. In their first report upon 38 cases they observed 4 pregnancies as a result of treatment. In Thaler's larger series of 147 cases of all sorts of menstrual disturbances treated by weak doses of the x-ray, there were 80 patients with amenorrhea and oligomenorrhea. Five of these became pregnant in the first month following the treatment, a striking result to be sure, provided the factor of chance or coincidence could be ruled out.

That the x-rays exercise a therapeutic influence in these cases of sterility combined with habitually delayed menses is unquestionable. In a larger personal series of 33 patients, over half have become pregnant. This shows an appreciable reduction over the result obtained in my first 12 cases previously reported.<sup>12</sup> Patients were included, however, that may have been unsuited for the treatment in this later series. On the other hand, it became clear that to exclude the factor of chance or accidental therapeutic success it was important to arrive at an answer to the following questions: (1) What proportion of women by and large have *delayed periods* and what proportion of these bear children? (2) What is the percentage of cases of *sterility associated with amenorrhea* in a fairly large number of women who apply for relief of sterility? (3) What is the natural *fertility* in relation to the *menstrual function* of a fairly large number of women who have borne children?

Soon after my first publication I began to include patients with scanty periods and others in whom the periods were habitually delayed for shorter intervals, i.e., five, six, and seven weeks.

In spite of a more general adoption of x-ray treatment in these cases, no large statistical investigation appears to have been made in order to establish the natural incidence of sterility in this group of women or its proportion to normally menstruating women. Knowledge of the aver-

age expectancy for childbearing in any given case with reference to the menstrual function will prove helpful in estimating the aid rendered by any therapeutic agency, medicinal, hygienic, operative or x-ray.

In my first article<sup>12</sup> I attempted to arrive at these points by going over a relatively small number of cases. Twelve patients were subjected to ovarian x-ray irradiation, and pregnancy resulted in 9, or 75 per cent. Two questions naturally arose: (1) May this not have been a particularly favorable group of patients? (2) Would a larger series corroborate these findings? Meanwhile the discovery of a female sex hormone had aroused the hope that perhaps we were on the verge of a hormonal substance comparable in potency to thyroid extract or insulin which would naturally supplant the use of x-rays. For the past two years I have practically abandoned x-ray ovarian irradiation, awaiting the production of an ovarian or ovarian pituitary extract for therapeutic use.

The patients forming the basis of the present study came for the relief of delayed periods per se or because of sterility with which delayed periods happened to be associated.

General incidence of delayed periods (*opsomenorrhoea*, *oligomenorrhoea*).—It is interesting to compare the actual conceptional childbearing incidence of this group with the chances of conception and childbirth in the general female population. The general incidence of sterility is about 15 per cent according to the best statistics, i.e., at least 85 per cent of the married population have offspring. Of the total number of married women in the present series who had delayed menstrual periods 70 per cent were sterile and 10 per cent more were relatively sterile (this group having conceived once or twice terminating either in miscarriages or in a solitary full-term child). It is at once seen that the average normally menstruating woman has at least 5 times the better chance of becoming a mother than has the woman whose menses are habitually delayed or scanty or both combined.

Since these figures are taken from a private practice, in which perhaps one group of patients may predominate, I have analyzed 1044 consecutive cases from the Gynecological Service of Mt. Sinai Hospital to note their occurrence.\*

- 742 had normal menses.
- 201 had menorrhagia.
- 38 had scanty flow (*hypomenorrhoea*).
- 24 had delayed periods with normal flow  
(*opsomenorrhoea*, *oligomenorrhoea*).
- 10 had menometrorrhagia.
- 15 had delayed and scanty menses.
- 9 had delayed and profuse menses.
- 5 had periods every twenty-one days.

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\*I am indebted for these statistics to the Resident House Gynecologist, Dr. B. Urdan.



It will be seen that 87 out of the 1044 patients, or 8 per cent, had either delayed or scanty periods or a combination of both. In 9 patients the periods were both delayed and profuse. In other words, in a general gynecologic service, 8 per cent had some delay or slowing up of the tempo of the menstrual cycle with or without a definite change in the quantity of the menstrual flow.

If we analyze these cases from the viewpoint of their fertility in relation to the menses, we find in the 742 patients with normal menses:

- 62 had no children, or a primary sterility of 8 per cent.
- 59 had 1 to 3 abortions or a secondary sterility of 8.7 per cent.
- The total sterility for this group was 16.7 per cent, and 8.7 per cent were pregnant once to three times, terminating in abortion.
- 113, or 15 per cent, had 1 child and no abortions.
- 37, or 5 per cent had 1 child and 1 to 3 abortions.
- 471, or 63.7 per cent, had 2 to 14 children.

As no data with respect to voluntary or involuntary sterility were obtained, the average relationship may be assumed for this series.

#### HYPOMENORRHEA GROUP—38 CASES

- 13, or 33½ per cent, had no children (3 of these had 1 miscarriage each).
- 1 had 4 miscarriages.
- 7 had 1 child with or without a miscarriage (one of these had 12 miscarriages).
- 17 had 2 children or more.

#### DELAYED PERIODS BUT PROFUSE—9 CASES

- 2, or 22 per cent, had no children.
- 2 had 1 child only.

#### HYPOOLIGOMENORRHEA—15 CASES

- 5 out of 14, or 36 per cent were sterile.
- 3 had 1 or 2 miscarriages, a primary and secondary sterility of 55 per cent.
- 2 had 1 child.

#### OLIGOMENORRHEA—24 CASES

- 5 out of 14, or 36 per cent, were sterile.
- 4 were secondarily sterile.
- 9 were primarily or secondarily sterile, a total sterility of 37.5 per cent.

#### MENORRHAGIA—201 CASES

- 20 out of 201, or 10 per cent were sterile.
- 75 out of 201 had 1 miscarriage or 1 child with or without miscarriages.

The total number of children are reckoned against the miscarriages and sterility in the different groups and the results are shown in Table I.

TABLE I

TYPE OF MENSES	NO. OF CASES	PRIMARY STERILITY AND SECONDARY STERILITY, WHERE ONE CHILD WAS BORN WITH OR WITHOUT A MISCARRIAGE				WOMEN WHO BORE 2 OR MORE CHILDREN, WITH OR WITHOUT MIS- CARRIAGES			
		PATIENTS	CHILDREN	MISCARRIAGES		PATIENTS	CHILDREN	MISCARRIAGES	
Normal menses	742	271	150	95		471	1438	223	
Menorrhagia	201	95	58	32		106	478	88	
Hypomenorrhea	38	20	7	6		18	60	26	
Menometrorrhagia	10	5	1	0		5	16	5	
Delayed but profuse	9	4	1	0		5	16	3	
Hypooligomenorrhea	15	8	1	4		6	19	2	
(habitual delay of 5 to 8 weeks)									
Oligomenorrhea	24	7	2	2		17	51	2	
(8 patients had habitual delay of 8 to 24 weeks, and altogether these had 9 children or only 11.3%)						Of the 60 children borne by the 18 patients in the hypomenorrhea group: 2 had 10 children each 2 " 6 " " 4 " 4 " " 10 " 12 " altogether			

The striking difference in this analysis is in the patients who were either totally sterile or who had one child or one or two miscarriages as against the patients who had two children or more. Thus in the normally menstruating group there were 271 patients with 150 children and 95 miscarriages, i.e., a fertility of 55 per cent with 30 per cent miscarriages; whereas in the patients with the delayed or scanty menses or a combination of both of these, 38 in number, there were altogether 11 children and 25 miscarriages, or a fertility of 29 per cent, while the miscarriages were appreciably increased, i.e., to 66 per cent.

The menometrorrhagia group showed 5 patients with but 1 child and no miscarriages, again showing a marked reduction in the fertility.

Comparison between the normally menstruating group in patients who had no children or less than two children shows:

Normal menses: 271 patients, 150 children, 55 per cent fertility.

Disturbed menses: 43 patients, 12 children, 27 per cent fertility.

Of the whole group of 1044 patients, 104 were primary sterilities or about 10 per cent, and 301 were secondarily sterile, or 29 per cent.

We also see that about 30 per cent of the 1044 patients (or 310 patients) showed some abnormality in menses, at least 22 per cent being of the menometrorrhagia group.

The relative degrees of amenorrhea were found to bear a definite relationship to the sterility. For example, of the 15 patients with hypogonadism, 12 (six to eight weeks' delay) bore a total of 12 children and had 5 abortions; whereas 3 (eight to twelve weeks' delay) had no children and only 1 abortion.

Of the 24 patients with oligomenorrhea there were 13 patients with the menses delayed for from five to six weeks. These bore a total of 32 children and had 8 abortions. There were 3 patients with a delay of seven to eight weeks, with 5 children altogether and no abortions. There were 8 patients with a delay of eight to twenty-four weeks with 9 children and no abortions. If we deduct from the last group the one patient who bore 6 children, there remain 7 patients of whom 3 had children.

Schroeder found that one-fourth of all gynecologic cases treated by him at Kiel showed some irregularity in the periods. The cases with delay from five weeks and over formed 6 per cent of his polyclinic patients taken for a period of two years (1924 and 1925), i.e., 482 out of 8085 patients, and 5 per cent of his private patients for the same two years, i.e., 47 out of 966 patients.

Comparisons with other groups were not available. Unfortunately the conceptional and birth incidence of Schroeder's cases are not given. It is hoped that such statistics will be forthcoming from other clinics, since they will help us to formulate better therapeutic and prognostic conclusions. The statistical study here presented by no means covers a number of points which might prove of interest and value.

THE NATURAL INCIDENCE OF PREGNANCY IN THE UNTREATED CASES OF  
DELAYED AND SCANTY PERIODS

In the 77 cases of the Mt. Sinai Hospital gynecologic material comprising oligomenorrhea (24 cases), hypomenorrhea (38 cases), and hypooligomenorrhea (15 cases), there was a total of 23 sterile women, or about 30 per cent. If we include the three women who became pregnant once or twice but did not bear a full-term living child, we shall have a total of 37 per cent of sterile women. The longer the habitual delay the less they were likely to conceive. The majority of these patients fell into the group having their menses every six to eight weeks.

In my first publication I found 3 out of 54 who became pregnant without having received any treatment for the abnormal menses or for the sterility. It must be emphasized, however, that in those cases the intervals of delayed menses were longer than three months as a rule. Cases of shorter intervals of delay were included later on, as it was thought x-ray treatment might benefit these as well. Such benefit does not appear to have followed.

One hundred and sixty-seven patients with habitually delayed menses were carefully analyzed with respect to the length of delay. In 75 of these the periods were delayed as a rule from six to fifteen weeks. In 35 patients from sixteen weeks to nine months, and in 5 the delay was greater than nine months. There were 12 patients with delayed and scanty periods of which 5 noted their delay as between six and fifteen weeks and 7 between sixteen weeks and nine months. The others had periods of delay up to six weeks.

That hypofunction is a cause of sterility is borne out by the high percentage of childless women in this series. Of the 167 patients 147 were married women of whom 102 were sterile, almost 70 per cent; 18 more were relatively sterile. In other words 82 per cent of these patients had lowered fertility, or sterility. The relatively sterile women had conceived but did not carry to full term, or having borne one child, failed subsequently to become gravid. Therefore, a few cases of one child sterility are included in this study.

Of the 167 patients with habitually delayed menses, 148 were married. Thirty became pregnant. Of these 9 had one miscarriage, 10 had only 1 child each, 7 had 2 children, 3 had 3 children, and 1 had 4 children. If we include the 19 patients who were pregnant only once, the latter terminating in a full-term child or in a miscarriage, there are left 11 patients out of 148 who had 2 or more children. In other words there was a primary sterility among these 148 patients with more prolonged delay of menses in 80 per cent, and a secondary sterility in 13 per cent, making a total of 93 per cent sterility.

The history with regard to the duration of the marriage in the sterile group and the interval of menstrual delay is drawn from 215 cases, shown in Tables II and III.

TABLE II. PRIMARY STERILITY WITH AMENORRHEA (154 CASES)

AMENORRHEA	NO. OF CASES	MARRIAGE	NO. OF CASES
A. Patients with one period of amenorrhea (18 cases)			
3 to 6 months	4	1 to 3 years	8
1 to 2 years	5	4 to 15 years	10
4 to 15 "	9	and longer	
None of this series became pregnant without treatment.			
B. Habitual Amenorrhea (136 cases)			
Under 1 month	14	Under 1 year	13
1 to 3 months	58	1 to 2 years	22
3 to 6 "	40	2 to 3 "	22
6 to 12 "	24	3 to 5 "	38
Of these patients only 2 became spontaneously pregnant		5 to 20 "	51

TABLE III. RELATIVE STERILITY WITH AMENORRHEA (61 CASES)

	DURATION OF AMENORRHEA	NO. OF CASES
A. Patients with only one period of amenorrhea	4 months	1
	9 "	4
	1 year	1
	1½ years	3
	2½ "	1
	3 "	1
B. Patients with habitual amenorrhea	Under 1 month	8
	1 to 3 months	21
	3 to 6 "	12
	6 to 10 "	9
Two out of this series became spontaneously pregnant.		

#### THE INCIDENCE OF DELAYED MENSES IN RELATION TO PREGNANCY IN A SERIES OF 600 CONSECUTIVE OBSTETRIC CASES

There were 425 patients with normal menses.

There were 175 patients with irregular menses. Of the latter, 140 patients gave a history of habitual delay. The delayed menses of these 140 patients were grouped as follows:

Under 1 month	82 cases
1 to 2 months	30 "
2 to 4 "	20 "
5 to 12 "	8 "

As these 140 cases include 33 patients treated with x-rays, it leaves 107 patients that became spontaneously pregnant out of the 600, or a fertility of 18 per cent. If, however, we deduct the 82 patients whose menstrual delay was under a month, we have left 25 patients whose menstrual delay was habitually longer than a month and though not treated for the condition became pregnant, giving them a 4 per cent fertility. It is obvious that the greater the delay in the menstrual periods the smaller will be the percentage of gravid cases.

#### DYSMENORRHEA ASSOCIATED WITH DELAYED MENSTRUATION

It is interesting to note that of 167 patients, 21 or 12.5 per cent complained of dysmenorrhea. The menstrual pain, however, was mild in the majority.

In 53 patients or 32 per cent the onset of menstruation was given at the age of fourteen or later.

#### EXCLUSION OF OTHER CONTRIBUTING FACTORS

The possibility of the tubes as a causal factor was checked in 106 of the 167 cases. Nonpatency of the tubes was found in 13 per cent of these cases. This is in marked contrast to the general occurrence of closed tubes in otherwise normally menstruating women treated for sterility in whom we have found at least 33, 39 per cent of closed tubes. The peculiar relative immunity that these women enjoy invites speculation. One explanation may here be offered at least, and that is that infections are more liable to occur during menses and the opportunity is less in women who menstruate infrequently.

Another important factor as a cause of sterility, namely the male, could also be excluded because in most of these cases the male was found to be potent as judged by the quality and quantity of his semen (condom and Hühner tests).

#### TREATMENT

From the foregoing relationship between hypoovarian activity and sterility, it readily follows that any form of treatment must necessarily have for its purpose the stimulation of ovarian function, thereby improving the chances for fertility.

#### RESULTS OF REPLACEMENT THERAPY

The preparations of gland extract in common use, such as ovarian residue, varium, agomensin, corpus luteum, thyroid extract, and anterior pituitary were also employed in these cases. Sometimes calcium lactate and calcium chloride were added on the basis of some connection between ovarian hypofunction and disturbed calcium metabolism. In other cases, an attempt was made to improve the general health of the individual by the usual measures of diet, hygiene, and tonics. In 57 cases such therapy was used with practically no effect. There was an improvement of function followed by pregnancy in only 2 cases observed over a period of years, but whether this was due to the treatment it is difficult to say.

Pregnancy occurred in 10 patients who received gland extracts in one form or another. Four of these patients became pregnant during the amenorrhœic phase so that it was not possible to compute the expected date of labor. By carefully noting the duration of gestation in all these cases in the future some idea may be obtained as to the relation between the ovulation preceding the conception and the last preceding menstruation.

Since it is possible to assay ovarian extracts containing the active principle according to more recent pharmacologic methods, a number of preparations here and abroad have offered better prospects of success. Of the foreign products, progynon, menformon or follicular panhormon, hormova, and glandofoli are produced on a pharmacologic

basis (on the mouse unit system). Oestrogen and amniotin are American products which are elaborated on the same principle. The effect upon human females has so far not satisfied expectations. Apparently effects upon mice cannot be reproduced in human beings. Conditions in the mouse are obviously very different from those in the human. As Novak well says, we are dealing with a healthy animal whose uterus, if immature, is nevertheless susceptible to maturity. So far I have not seen improvement or restoration of menstrual function in my own cases, but it is possible that I put these organic extracts to too hard a test in advanced cases of amenorrhea. Prolan (Zondek) represents an extract of anterior lobe pituitary. This is supposed to support the action of progynon. The hypophysis has been proved experimentally to be a powerful stimulant to the ovaries. Emmenagogues, such as potassium permanganate, apiol, yohimbin, salipyrin, aloes, and cathartics, are still recommended in combination with the older and new organic extracts. Their action is most probably through the increase in pelvic hyperemia.

The relatively poor results obtained with opotherapy prompted us to resort in 1923 to x-ray irradiation of the ovaries. A striking improvement followed this treatment in 33 patients of whom 16 became pregnant shortly afterward.

Mild *hypophyseal irradiation*, especially in delayed, very weak or irregular periods, has proved of value. The menses become regular more or less permanently and more profuse. Dysmenorrhea is incidentally also cured. Novak ventures the opinion that this is due to the sense of satisfaction the patient derives from knowing that her menses have returned to normal.

The way in which hypophyseal irradiation stimulates normal menstruation is not clear; nor the manner in which *mild ovarian irradiation* accomplishes its end. Whether it is stimulating or destructive (as claimed by Holzknecht) is still a question. There is still uncertainty concerning the hormonal function of some of the elements of the ovary. That the follicle apparatus and corpus luteum produce an inner secretory substance is generally recognized. The action of the interstitial gland is still disputable. Finally, as L. Adler<sup>23</sup> intimates, whether there exist one or several ovarian hormones is a matter awaiting solution.

We can agree with Novak that there is real danger of destroying through the x-rays the last remnant of the functional portion of ovarian tissue. Further, the theoretical damaging of the germ-plasm and eventually of the offspring which has, so far, not been demonstrated, is nevertheless not to be dismissed altogether. The babies born after treatment with mild x-rays, in my own experience have all proved, so far, to be normal in every way. There can be no question, however, that it is better to try the preliminary x-ray treatment of the hypoph-

ysis before resorting to the ovarian irradiation, even though the former is also fraught with theoretical danger.

#### SUMMARY AND CONCLUSIONS

In ovarian hypofunction, the opportunity for fertilization is diminished in proportion to the reduced ovulation. Other contributing factors as tubal occlusion, male impotence, etc., must, however, be excluded as entering into the causation of the sterility. We have shown in this study that the natural incidence of fertility is smaller in women with habitually delayed periods than in women who menstruate normally.

The material upon which the present analysis was based consisted of 1044 consecutive gynecologic cases from Mt. Sinai Hospital and 46 private gynecologic cases, 2200 private cases of sterility, and 600 private obstetric cases. The object of the study was to determine the occurrence and incidence of habitually delayed menstruation, the sterility, and fertility attending it as compared with normally menstruating women of these three groups and the general population. It was found that the menses are habitually delayed or scanty in 3.5 to 8 per cent of gynecologic patients and in about 10 per cent of patients whose marriage is sterile. These patients are more apt to be sterile than the normally menstruating women, the primary sterility varying between 30 and 70 per cent; and the total sterility, including secondary sterility, amounting in some groups to as high as 93 per cent.

The longer the periods of delay the greater is the sterility percentage. Patients having periods of delay under a month have 5 to 8 times the better chance of conceiving than those whose periods are habitually delayed from four to six months. On the other hand, women who menstruate normally have, by these statistics, at least 12 times better chance than those whose menses are habitually delayed for a month and many times more the conceptional advantage over those whose menses are habitually postponed for longer periods.

Not only are primary and secondary sterility greater in those patients with hypo- and opsomenorrhea but their total fertility is considerably diminished in proportion to the reduced number of periods per year.

As both the delayed character of the periods, their paucity, and the associated sterility and reduced fertility are expressions of ovarian hypofunction, it follows that any treatment to be effective must be concentrated upon increasing or improving ovarian function. Restoring good nutrition, improving the general hygienic and psychic conditions of the patient, in other words, general constitutional improvement is the first prerequisite. Thyroid treatment in the deficient basal metabolic rates, the administration of ovarian extracts of proved potency of pituitary extracts, and emmenagogues are auxiliary agents. These



however, are efficacious in few cases so far on account of the relatively inactive products that are available. An ovarian extract containing a specific hormone in sufficient quantity to make up the deficiency in any given case has so far not been elaborated, but the future holds out a fair promise for success.

A more definitely proved and more efficacious physical agent is available in the use of x-rays. Small doses of the latter applied first to the hypophysis and if necessary to the ovaries have proved successful, not only in restoring the menstrual periodicity to more nearly the normal in 80 to 90 per cent of the patients, but it has also incidentally increased their fertility to at least 50 per cent. The theoretical damage of germ-plasm which is supposed to result from this treatment has, so far, not been demonstrated. Nevertheless, it appears highly desirable to supplant this treatment by a specific endocrine product whose potency should compare to insulin for example. From the more recent indications it may prove to be a combination of ovarian with pituitary extract. The hormone or hormones need not necessarily be isolated from the ovaries or hypophysis themselves but more conveniently and in adequate quantities from excretions and secretions in which they have already been abundantly found, as well as in the placenta.

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911 PARK AVENUE.

# A REVIEW OF BREECH DELIVERIES DURING A FIVE-YEAR PERIOD AT THE SLOANE HOSPITAL FOR WOMEN\*

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THE infant mortality in breech births has not been decreased. This is shown by a study of our own cases and a review of the recent literature.

The belief that the constant critical study of large series of cases, the methods used, the mistakes made, and the end-results obtained, will aid in decreasing this mortality, is our reason for presenting this paper.

Since 1920 the majority of stillbirths and neonatal deaths at Sloane Hospital have had careful autopsies under the direction of Professor W. C. Johnson. His findings agree with the constantly increasing

TABLE I. FIGURES SHOWING MORTALITY IN BREECH BIRTHS AS REPORTED IN RECENT YEARS

Pierson, Sloane	1923	12 %	
Lang, Frankfurt	1911-1926	13.1 %	
Heidler, Vienna	1920-1926	11.45 %	
Holland, London	1922	9.6 %	(definitely due to breech delivery)
Poulain, Paris	1922-1926	11.05 %	
Ridler, Australia	1926	13 %	(gross)
Irving and Goethals, Boston	1926	9.78 %	
Rasmussen, Oslo	1926	14.2 %	(gross)
		21 %	(gross)
Gibberd, London	1927	13.7 %	(corrected)
King and Gladden, New Orleans	1928	10.12 %	

number of autopsy reports and confirm the opinions of Van Reuss, Holland, Ehrenfest and others, that in breech birth 75 per cent of the deaths of viable babies are due to birth injuries.

In 1923 R. N. Pierson reported our results for the years 1920, 1921, and 1922, giving a 12 per cent infant mortality among viable babies and the autopsy results in these cases.

The 348 cases reported in the present paper include all breech deliveries during the years 1923 to 1927 inclusive. Ninety-two of these babies were markedly premature or macerated, weighing under four pounds, and are briefly reviewed in Table II.

\*Read at the Fifty-fourth Annual Meeting of the American Gynecological Society, Old Point Comfort, Va., May 20-22, 1929.

TABLE II. REVIEW OF CASES DISCARDED FROM SERIES BECAUSE FETUS WAS MACERATED OR WEIGHED UNDER FOUR POUNDS

Toxemia of pregnancy	24
Cardiac	2
Pneumonia	1
Syphilis	9
Diabetes	3
Serious pyelitis	3
Placenta previa	1
Unclassified or undetermined	43
Living babies discharged from hospital in this group	6
Total	92

The largest babies in the entire group that were not macerated weighed 3 pounds 7 ounces, 3 pounds 5 ounces, 3 pounds 5 ounces, 3 pounds 13 ounces, 3 pounds 10 ounces and 3 pounds 14 ounces. In these cases there were no maternal complications and all the children lived.

In 256 cases, the babies were not macerated and weighed over four pounds. One hundred and thirty-three of these patients were primiparae, among which there were 11 stillbirths, a gross infant mortality of 8.3 per cent. There were 123 multiparae, with 25 stillbirths, a gross infant mortality of 20 per cent. A brief summary of the history, clinical and autopsy findings of each of these 36 deaths is appended, allowing each reader to compute his own net mortality from the gross figures. It will be noted that among these patients 4 had gross fetal abnormalities, 6 were markedly premature according to the menstrual history, 4 others were in cases complicated by placenta previa, and in 2 there were fibroids. In one there was presumptive evidence that the mother destroyed the baby. The majority of these cases were among the multiparae, which partly accounts for the high mortality in this group.

TABLE III. SUMMARY BY YEARS OF CASES OF STILLBIRTHS AT SLOANE HOSPITAL

UNCORRECTED MORTALITY 1923-1927				MORTALITY CORRECTED BY ELIMINATION OF BREECH DELIVERIES WITH FETAL ANOMALIES AND PLACENTA PREVIA		
	Primipara Per Cent	Multipara Per Cent	Total Per Cent	Primipara Per Cent	Multipara Per Cent	Total Per Cent
1923	11.5	16	14	11.5	13	12.5
1924	8	35	21	8	35	21
1925	8	22	15	8	16	12
1926	0	17	11	0	8+	5
1927	8	15	11	8	10+	8.9
5 year mortality	8.3	20	14	8.3	15.5	11.11
Maternal mortality 0.75 per cent, one case serious condition when admitted after 4 days of hard labor, shock and hemorrhage.				Maternal mortality 0.86 per cent, streptococcus, hemolytic, septicemia.		
	TOTAL CASES			STILLBIRTHS		MORTALITY Per Cent
Placenta previa	4			3		75
Prolapsed cord	12			8		66 $\frac{2}{3}$

Gross mortality 14 per cent  
 Eliminating fetal abnormalities inconsistent with life and placenta previas 11.1 per cent

It is difficult to evaluate briefly the net mortality figures from published reports, as each author has his own standard for reaching this figure. Many authors in giving net mortality statistics eliminate all such cases as those reported above, and some still further reduce their mortality by eliminating those cases complicated by toxemia of pregnancy, contracted pelvis, or prolapsed cord. In many of the older statistics as well as in some of the recent figures neonatal deaths are eliminated. The gross mortality in these 256 cases, including all stillbirths and neonatal deaths, is 14 per cent. Even eliminating the 4



Fig. 1.—Under deep anesthesia especially with a moderate Trendelenburg position it is possible to push the presenting part out of the birth canal.

cases of gross fetal abnormalities inconsistent with life, and possibly the serious placenta previas, we would still have a net mortality of 11.1 per cent.

Sloane Hospital is a teaching institution. A large number of undergraduates are constantly being instructed as well as a large intern staff which serves for a period of one year, and a resident staff which serves for three years longer. It has been our aim to teach the undergraduate students the principles of obstetrics and the prevention and recognition of the various complications. They examine as many women as possible and deliver some normal cases. They see the opera-

tive deliveries and have impressed upon them the dangers to the mother and child of operative interference and the necessity of much further training before they are capable of doing such procedures. It has been our policy, on the other hand, to allow the carefully selected intern staff and a resident staff selected from the interns to do as many of the operative procedures as possible, under supervision. Twelve or 15 attendants also have the privilege of delivering cases in the hospital. An average of 18 different operators have taken care of the breech deliveries each year. The least experienced of these operators have handled the multiparae under the false impression that they were

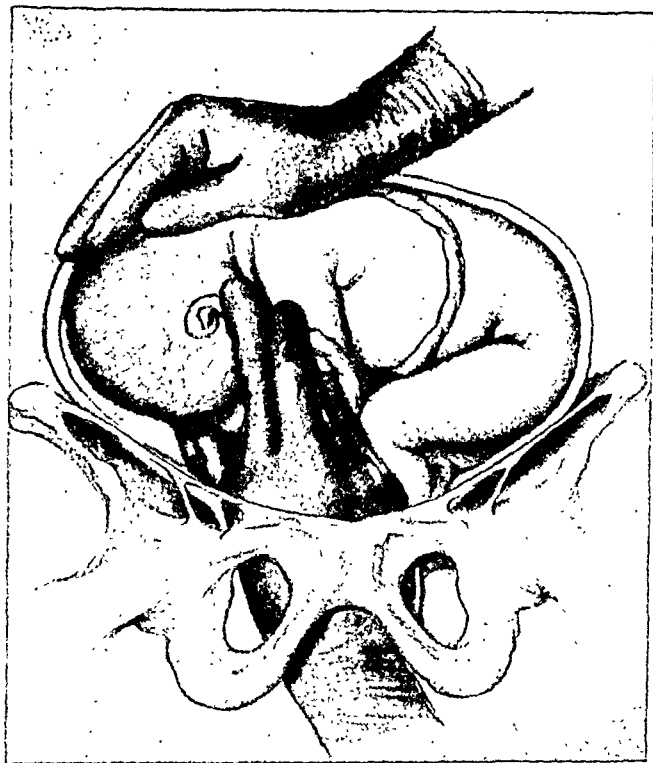


Fig. 2.—The birth canal is available for various manipulations. The feet can be found easily and reduced and the cord loosened, preventing shock to the child or separation of the placenta. The arms can be folded on the chest or a fillet applied.

the easiest cases. Tables III, IV, V, and VI summarize briefly the cases in which stillbirths occurred.

A very large proportion of the infant mortality in breech births occurs among macerated, abnormal and premature children and also in cases of multiple birth. This mortality will be reduced by better prenatal care.

External version is being more and more advocated. We agree with Bartholomew who recently discussed the subject before this Society, as well as with Ryder, Gibberd and many others who have advocated routine version in properly selected cases at the eighth month of pregnancy, and feel that with greater experience more of these cases can

TABLE IV. SUMMARY OF STILLBIRTHS AND COMPLICATIONS FOUND AMONG THE PRIMIPARAE

63 per cent stillbirths autopsied	{	4 Intracranial injury
		2 Other injuries
		1 Congenital pneumonia
37 per cent stillbirths not autopsied	{	3 Probable intracranial injuries
		1 Probable congenital pneumonia
		1 Probable fracture of neck
55 per cent of mothers had abnormal pelvis		
82 per cent had some difficulty with cervix		
27 per cent prolapsed cord		
36 per cent premature rupture of membrane		
18 per cent prolonged labor		
The largest baby in this group weighed 8 pounds 13 ounces. In one case the mother had toxemia of pregnancy, induced labor and the child died from prematurity.		
Gross mortality in primiparae		8.3 per cent
Corrected mortality		7.5 per cent

TABLE V. SUMMARY OF STILLBIRTHS AND COMPLICATIONS FOUND AMONG THE MULTIPARAE

66 per cent of stillbirths autopsied (17)	{	12 Intracranial injury
		3 Congenital pneumonia
		3 Other injuries
		4 Spinal injuries
		1 No cause of death found
		2 Congenital anomalies
32 per cent of stillbirths not autopsied	{	3 Probable intracranial injuries
		2 Probable congenital pneumonia
		2 Probable congenital anomalies
32 per cent of mothers had abnormal pelvis		
40 per cent had some difficulty with cervix		
20 per cent had prolapse of cord		
42 per cent had early rupture of membranes		
12 per cent had placenta previa		
20 per cent had prolonged labor		
16 per cent fetal anomalies		
16 per cent abnormally large babies weighing 10 pounds 5 ounces, 10 pounds 9 ounces and 11 pounds 11 ounces.		

TABLE VI. ABNORMAL PELVIS AND PREMATURE RUPTURE OF MEMBRANES

	PRIMIPARA PER CENT	MULTIPARA PER CENT
1 Incidence of abnormal pelvis	18	22
2 Incidence of abnormal pelvis in cases with stillbirths	60	32
3 Incidence of abnormal pelvis in cases with ruptured membranes	23	32
4 Incidence of abnormal pelvis in cases with intact membranes	16	18

be turned and the infant mortality, which even now is under 2 per cent due to this operation, can be reduced. There are, however, a large number of cases which cannot or should not be turned.

The undilated cervix remains as the chief source of danger in breech deliveries. It will be noted that among our stillbirths, 82 per cent. of the primiparae and 40 per cent of the multiparae had trouble on

account of the cervix. The dilatable but not paralyzed cervix was the chief error in judgment. A "hands off" policy until the cervix is completely dilated of course should be the rule, but there are many cases where the cervix will not dilate even after prolonged labor. This is

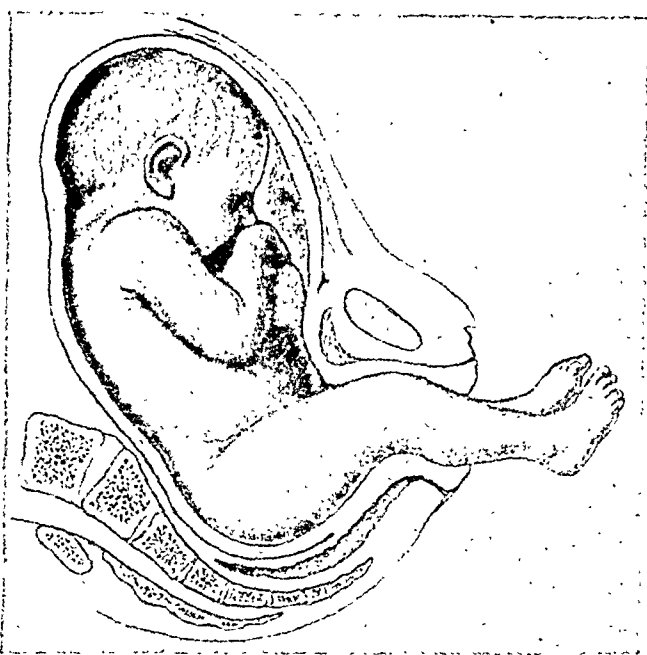


Fig. 3.—The buttocks brought to the hollow of the sacrum using all available space without angulation of the child's body.

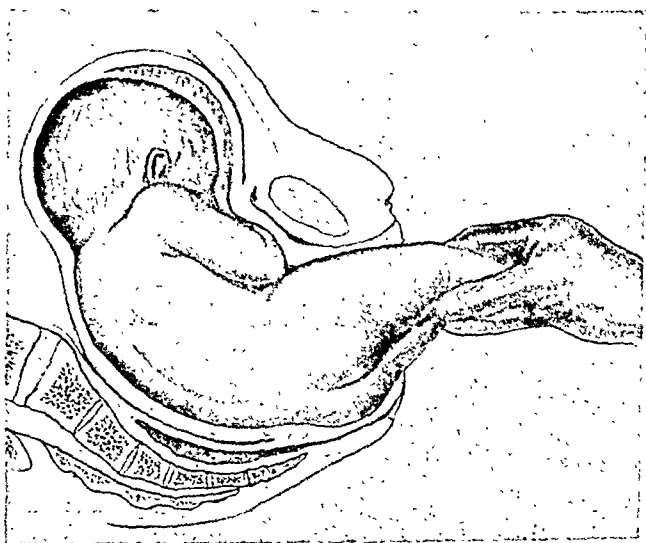


Fig. 4.—Gentle traction on anterior foot rotates buttocks into the direct antero-posterior diameter of the pelvis. After the birth of the buttocks, continued traction downward and forward brings the back parallel to the symphysis.

especially true in cases of contracted pelvis. Sixty per cent of our primiparae and 32 per cent of the multiparae in whom the cervix was a complication had contracted pelvis.

We dread the neglected case where the membranes have been ruptured for hours and where the cervix is undilated and the child compromised; bringing down one or both feet has not given satisfactory results. In 22 cases where the bags were used there were 5 stillbirths. Even the largest bags did not give complete dilatation and the paralysis of the cervix necessary for a safe delivery. On the other hand, Zangemeister and Baer induce labor as a matter of routine with the

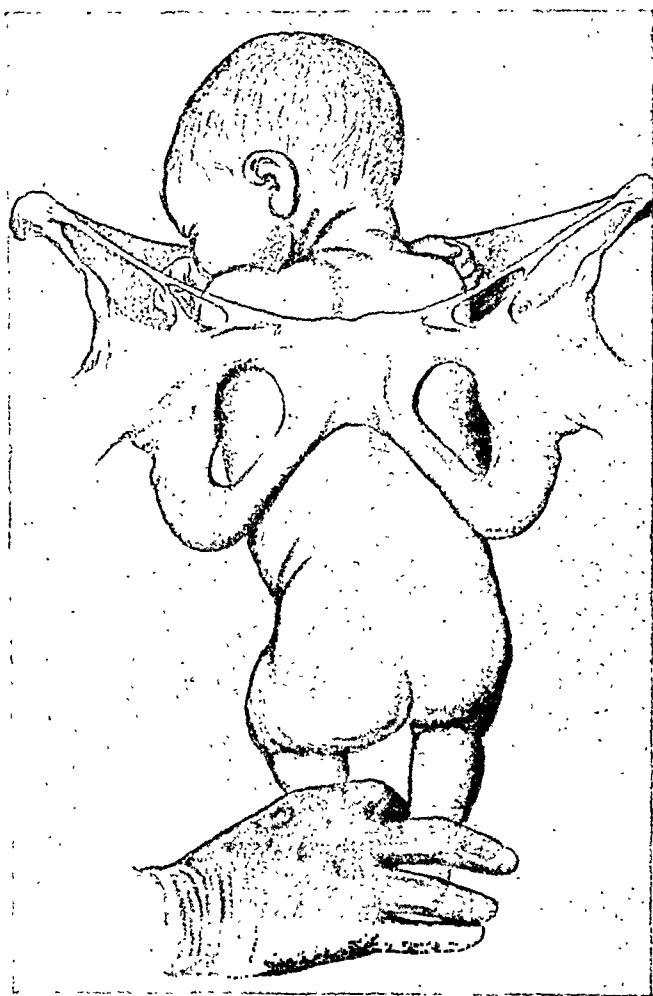


Fig. 5.—Continued very gentle downward traction engages the shoulders in the transverse diameter of the inlet. Extended arms in this diameter seldom cause much trouble.

aid of Zweifel's bag in all cases with contracted pelvis and in many others. They report 88 per cent normal deliveries and a remarkably low infant death rate. We have always dreaded induction of labor in such cases.

Manual dilatation of the cervix is most unsatisfactory. Serious tears and imperfect paralysis are too frequent. Cutting of the anterior lip of the cervix should frequently be done in such cases, even in pla-



centa previa, as Essen-Möller has shown us. Occasionally one of the low cesarean sections is indicated. Due consideration must be given, however, to the large number of neonatal deaths due to congenital pneumonia in this type of case.

The Pomeroy bag, which is now rightfully discarded as a means of eliminating the first stage, has nevertheless frequently been found useful by us. When the cervix is soft and dilatable, it is a very satis-



FIG. 6.—When the shoulders have passed the inlet, by inserting the hand parallel to the symphysis one shoulder is pushed backward into the hollow of the sacrum. This prevents torsion of the body.

factory means of paralyzing the cervix and dilating the entire birth canal. We regret that the demand for this bag was so small that the manufacturers no longer make it.

The improper or careless handling of the first stage and the excessive use of the various sedatives to prevent pain increase the difficulty with the cervix.

Prolapse of the cord was found in 12 of the 256 cases, and 8 stillbirths resulted. Doctor Caverly of our service found in a previous series of cases 35 prolapsed cords among 6947 consecutive deliveries, 8 or 22.8 per cent having occurred in breech presentations. The mor-

tality in vertex presentations was only 26 per cent, while the mortality in the breech cases was 75 per cent, partly due to careless watching of the patient but mostly due to frantic efforts to deliver the baby at once. It should be easier to replace a prolapsed cord in a breech presentation than in a vertex and the proper use of bags and the necessary paralysis of the cervix before the extraction of the child should save more of these babies.



Fig. 7.—Traction downward and backward allows the shoulder to engage under the symphysis.

Many writers including Rasmussen, Irving and Goethals, as well as Piper and Bachman in their recent article, have advised the routine interference with the second stage under deep anesthesia. This allows the patient to be completely relaxed and placed in the most favorable position for the delivery. The soft parts can be properly prepared for the birth, permitting the operator to adjust the child to the birth canal and use all the available space without angulation of the child's body. He can loosen the cord, preventing shock to the baby or the separation of the placenta. It allows the operator to reduce the arms which are

frequently extended above the head as shown by Bonney, Potter and others, and which we can confirm by our own experience. It allows the operator to prevent impactions or to correct them with the minimum force when they do occur. Plenty of time should be taken in the various maneuvers, even though the child inhales amniotic fluid, as any undue force will surely kill it. Unquestionably, in the hands of individual operators the routine interference with the second stage gives



Fig. 8.—When one arm has been delivered and the other arm is high in the pelvis, the anterior shoulder can be pushed back into the birth canal, the head loosened at the brim, and the body rotated completely around so as to bring the other shoulder underneath the symphysis.

reasonably satisfactory results, saves time and suffering and prevents some complications. We followed this policy as a matter of routine for a short time but our mortality increased so greatly due to the misjudgment of the cervix and to various other complications which arose in the hands of the less experienced operators that we returned to the more conservative "hands off" policy with a marked reduction in the mortality. Even in normal labors where the child is born to the umbilicus, the delivery of the shoulders and after-coming head



Fig. 9.—When the arms are born, the body should be kept parallel to the woman's thigh and the shoulders should be pushed backward and upward into the birth canal. This permits the head to be loosened at the brim and flexed by external manipulation.

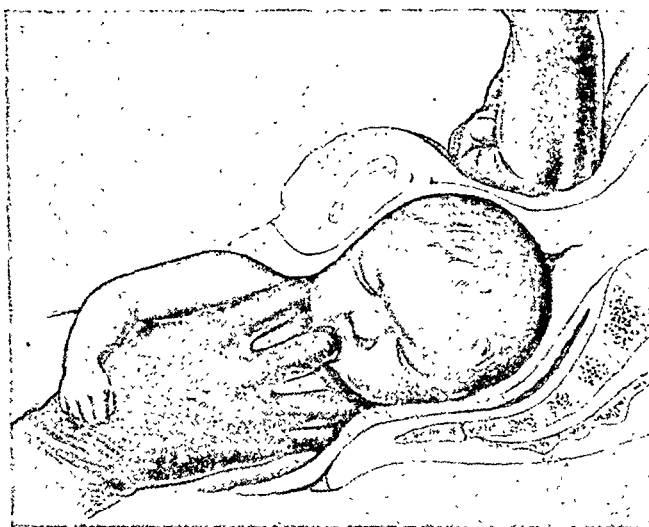


Fig. 10.—With the head well flexed and the occipital frontal diameter of the head in the transverse diameter of the inlet, external pressure pushes the head into the hollow of the sacrum. Excessive pressure ruptures the falx. Note the position of the mouth when the biparietal is in the hollow of the sacrum.

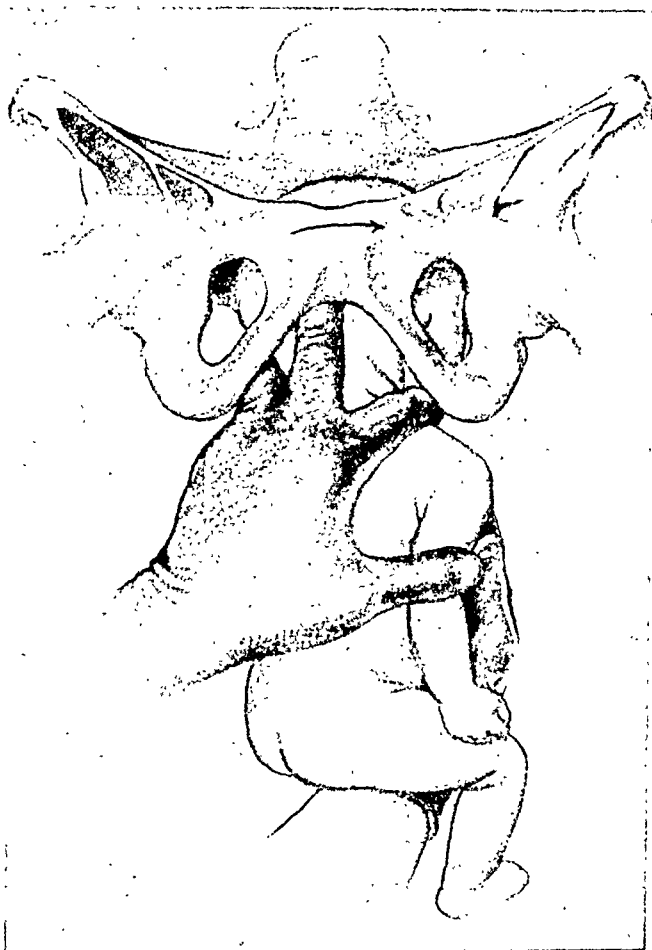


Fig. 11.—Rotating the child's body and head after the biparietal has reached the hollow of the sacrum.

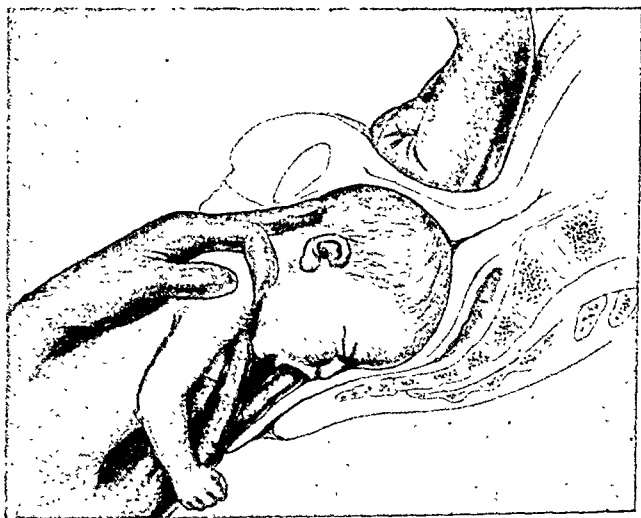


Fig. 12.—Protecting the child's neck by the large finger of the operator's hand until the occipital protuberance is underneath the symphysis. Piper's forceps can be advantageously used at this stage.

should be done under deep anesthesia, and precipitate deliveries must be guarded against, as shown in the summary of our cases.

We have seldom used forceps on the after-coming head. Undue pressure from above undoubtedly increases the biparietal diameter, frequently ruptures the falx and when the tentorium has been torn, forces the medulla oblongata into the foramen magnum. When such

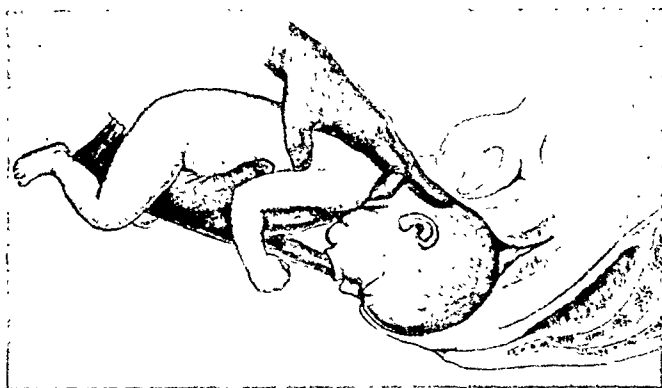


Fig. 13.—With the leverage on the big finger the entire body can be swung up without angulation of the neck.

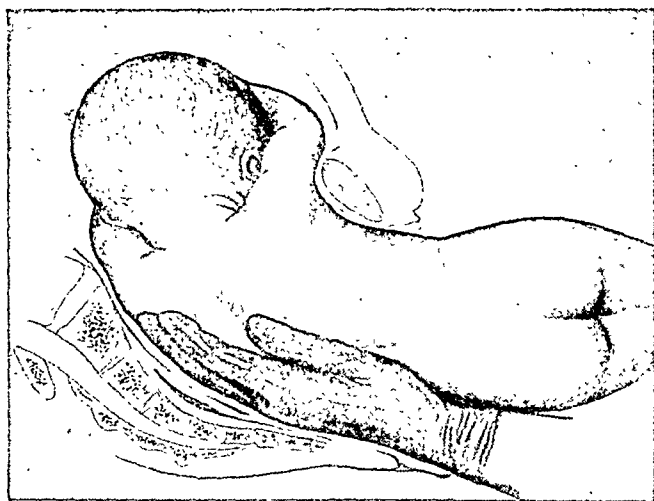


Fig. 14.—Reaching for the posterior shoulder high up in the pelvis results in dangerous angulations and traction on the child's body, causing Erb's palsy and hemorrhages into the cord.

force is necessary, the use of forceps will not save the baby. With large fat women, when the patient cannot be completely relaxed or when proper assistance is not available, the occasional use of the Barton forceps may help to bring the head down into the pelvis. These forceps slip on easily and have been used in 3 such cases by one of us. When the head is in the pelvis the Piper forceps is proving a very useful instrument.

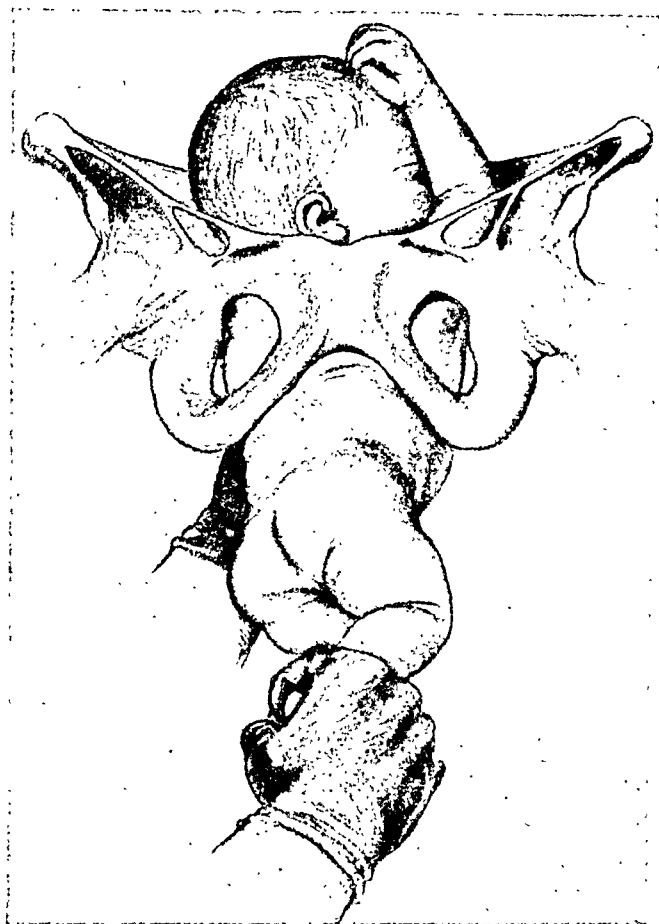


Fig. 15.—In impacted shoulders traction or rotation causes serious injury. It is safer to take plenty of time so as to push the shoulders above the brim where frequently the arms can be reduced or placed into the transverse diameter where they seldom cause trouble.



Fig. 16.—Dangerous twisting and angulation of the child's neck.

Table VII giving the ratio between spontaneous and operative deliveries is very interesting and is a great argument for the "hands off"

TABLE VII. QUOTING INCIDENCE OF SPONTANEOUS AND OPERATIVE DELIVERIES WITH THE INFANT MORTALITY IN EACH GROUP

CLINIC	BREECH CASES	SPONTANEOUS		OPERATIVE		TOTAL MORTALITY	CORRECTED MORTALITY
		PER CENT	PER CENT MORTALITY	PER CENT	PER CENT MORTALITY		
Rimey-Baudeloque 1890-1911	1302	76.3	9.52	18.7	25.8	18.8	
Cuny-Herff, Basel 1902-12	1389	89.9	3.6	5.1	16.9	10.2	
Guys Hospital, Gibberd 1927	221	61	Not stated	39	Not stated	22	13.7
Heidler, Vienna 1920-26	65	43	9.9	57	13	11.45	
Breslau Klinik Busse 1911-16	361	16.07	Not stated	84	Not stated	17.45	
Frankfurter Klinik Lang 1911-26	729	11	Not stated	89	Not stated	13.1	8.8
Ridler 1926		Fetal death rate in cases, including prematures, delivered by nurses, 5.4 per cent					
		Fetal death rate in cases, including prematures, delivered by residents, 19.1 per cent					

policy in breech births. Still even in the most conservative clinics a very large proportion of the cases end in operative interference and the mortality in such cases is very high.

In view of such a large infant mortality, of the prolonged labor

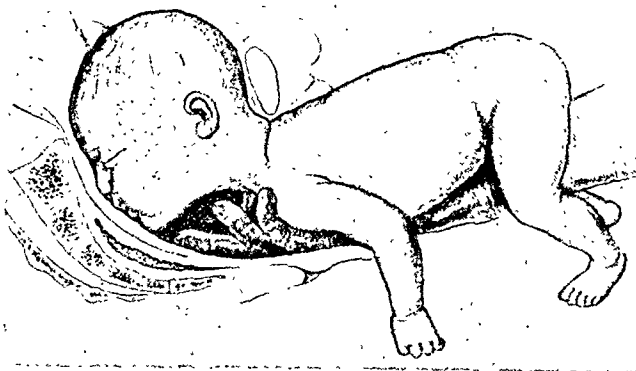


Fig. 17.—Dangerous angulation of the child's neck by too early rotation of the head.

which is frequently necessary to deliver such cases safely, and of the serious complications often involved, it is not surprising that many individual operators, especially among the general surgeons, are resorting more and more to cesarean section as a quick and easy way out of the difficulty in breech presentations. Some of our stillbirths could have been saved by cesarean section but its frequent use will undoubtedly increase the maternal mortality and is unnecessary in the vast



majority of cases. Cesarean section is indicated in the elderly primipara if any difficulty with the delivery is foreseen. Repeated breech presentations in the same woman are comparatively rare. This should be taken into account with young women whose future pregnancies might be jeopardized. In cases of contracted pelves, cesarean section should be seriously considered not only on account of the unmoulded after-coming head but also on account of the difficulty in dilating the cervix.

Crothers as well as Ehrenfest has recently stressed the birth injuries among babies that survive breech delivery. The reports from our follow-up clinic show a surprisingly small number of such cases. Comparing this series with those reported by Pierson in 1923, we find that we now have fewer broken necks, and that the injuries are not as extensive as in his series.

The accompanying figures show the technic advocated by us in order to avoid angulation and torsion of the child's body, cord complications, and breech impactions.

#### CONCLUSIONS

In order to decrease the infant mortality we would emphasize the necessity of:

1. Better prenatal care including external version in proper cases.
2. The thorough study of each individual case, multipara as well as primipara, in order to anticipate complications as much as possible.
3. Greater use of the cesarean section in elderly primiparae and in contracted pelves where not only the unmoulded after-coming head but difficulty with the cervix must be considered.
4. A "hands off" policy as long as the labor is advancing.
5. Constant watchful care throughout the labor to prevent complications or to interfere when they occur, using sedatives with great caution.
6. In breech extractions, sufficient time should be taken under deep anesthesia to prepare the birth canal, to prevent torsion and angulation of the child and to prevent and correct impactions gently. The cord can be compressed or even cut without great danger to the child.

*(For discussion, see page 720.)*

# THE ACTIVE IMMUNIZATION OF PREGNANT AND PUERPERAL WOMEN WITH STREPTOCOCCAL TOXINS AGAINST STREPTOCOCCAL PUERPERAL FEVER

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NOTWITHSTANDING the many advances in the prevention and management of obstetric complications and sequelae, the incidence of streptococcal puerperal fever with its mortality and morbidity still remains high. It is for this reason that further investigations are necessary to devise prophylactic and therapeutic measures to combat this disease. The appalling mortality of puerperal fever of former centuries, especially that during the time of the beginning of maternity hospitals, is too well known to require elaboration. These unfavorable conditions continued to be universal until 1847, when Semmelweis introduced antiseptic measures and decreased the mortality in his own clinic from 11.4 per cent to 1.27 per cent. However, it was not until 1870, when Lister firmly established the principle of antisepsis, that Semmelweis' conception was generally accepted. Notwithstanding the general dissemination of the knowledge of antisepsis and later asepsis, there has been since the beginning of the twentieth century, no appreciable decrease in the puerperal morbidity and mortality. In the volume of unprejudiced mortality statistics published in July, 1926, W. C. Davis, Chief Statistician of the Census Bureau, reports that the United States has a total puerperal mortality rate of 68 to 10,000 births, one-half of which is due to sepsis and eclampsia. According to the census bureau we have an estimated population of 111,000,000 with an annual birth rate of 2,500,000 which means that 8,500 women die each year from puerperal fever or eclampsia, both preventable diseases. However, it should be understood that the rates in the United States include the colored race, which still shows a total mortality of 111, a puerperal sepsis of 38 and deaths from other puerperal causes of 73, or nearly double that of the white mothers included in the calculations. That we still have much to achieve is realized from the fact that a bulletin of the Children's Bureau at Washington places us in regard to maternal welfare fourteenth in a list of seventeen civilized nations (our maternal mortality rate being exceeded only by Belgium, Spain and Switzerland). Also one must not forget the thousands of women that become invalids as a result of puerperal infections; it is said that for every woman that dies five suffer from it.

That the streptococcus is responsible for most of the puerperal infections and especially those ending fatally, is generally known. (Bigger and Fitzgibbon, Colebrook, Harris and Brown.) It is for this reason that all efforts have been directed to the immunization of pregnant and parturient women against streptococcal infections. The first work in prophylactic immunization against streptococcal pelvic infections was performed by Bumm in 1905 with killed streptococci. Of the 5 patients he injected prior to operation for uterine carcinoma 2 died from postoperative shock and hemorrhage, while in the remaining 3, a feverless and smooth convalescence followed. Polano, in the same year, published his results of active immunization in obstetric and gynecologic patients. He obtained the strains of streptococci from patients with erysipelas, scarlet fever, puerperal fever and angina. After centrifuging the ascites broth cultures and killing the organism, he utilized the sediment taken up in sodium chloride solution. By means of this bacterial suspension he succeeded in protecting mice and dogs against fatal doses of streptococci. He then immunized 60 obstetric and gynecologic patients who were operated upon without a death. Although Polano drew no definite conclusions, he considered his results a basis for further work.

Levy and Hamm in 1909, cultivated streptococci from puerperal fever patients (whether from the blood or cervix is not stated) in ascites glycerine bouillon. The sediment of this culture was added to 5 c.c. of immune serum (polyvalent), thoroughly shaken and then allowed to remain for three hours in order for the immune bodies to become fixed to the bacteria. The organisms were then killed by a phenol solution. The mixture was centrifuged and washed repeatedly and suspended in normal saline solution so that each cubic centimeter of the suspension contained 50,000,000 streptococci. One cubic centimeter of the sensitized vaccine was given eight to ten days before delivery. Fourteen pregnant women were immunized by this method. The puerperium was afebrile in all the cases except one, in which a peritonitis occurred following a long labor. The peritoneal infection was secondary to a parametrial abscess due to *B. coli* and *Staphylococcus albus*. Levy and Hamm also used this sensitized vaccine therapeutically but only in a small group of patients, so that no valid conclusions could be drawn from either series.

In 1911, Watters and Eaton reported the use of polyvalent and autogenous vaccines in the active infectious stage. No details were given as to the preparation of the vaccine.

Champtaloup suggested in 1914 the active immunization of expectant mothers against streptococcus puerperal fever when the infection occurs in epidemic forms in institutions or in private practice when the home surroundings are dirty. He used three doses of a vaccine which were given at intervals of two days, in amounts of 100,000,000; 250,000,000, and 500,000,000 organisms.

Further studies of prophylactic immunization were reported by Jötten in 1917. He used six strains of streptococci isolated from the blood of six severe streptococcal puerperal fever patients. The washed bacteria from glycerine agar plates after one to two days' cultivation were utilized, and they were killed by heat. Later, he substituted 1 per cent glucose broth instead of glycerine agar and centrifuged the cultures to obtain the organisms. The bacteria were washed several times with normal saline solution before the final suspension was made and counted. A phenol preservative was added. He immunized 819 women from October, 1915, to April, 1916, injecting 25 to 50 million bacteria prior to parturition. Of this group of patients 131 or 16 per cent developed a fever above 38° C. axillary. From May to July, 1916, 433 pregnant women received 100 million bacteria and 58 or 13.3 per cent developed fever. From August to October, 1916, three hundred pregnant women were immunized with 250 million organisms and 32 or 10.66 per cent de-

veloped fever. From November, 1916, to March, 1917, 126 women were immunized with 500 million organisms and 9 or 7.1 per cent developed fever.

Jötten studied the vaccinated pregnant women serologically to determine the presence of specific antibodies by the bacteriotropine method of Neufeld and the opsonic index method of Wright. These methods demonstrated that a beneficial action resulted from the vaccinations, especially when the larger dose of 500 million streptococci was used. He also employed the method of Koch and Kleine to determine the presence of agglutinins, since these investigators found agglutinins in individuals receiving streptococcal vaccines. The results of Jötten indicated that vaccination with a streptococcus not only conferred an immunity against the puerperal fever strains but also against strains from other sources.

In 1922, Louros, immunized a series of pregnant women with a vaccine of washed streptococci obtained from nine sources (six from the blood of puerperal fever patients, two from surgical streptococcus infections, and one from a patient with erysipelas). One-half cubic centimeter (250,000,000 streptococci) was injected twenty days before the expected labor and 1 c.c. ten days before. No general reaction or increase in temperature was observed but local redness was noted. Of 151 pregnant women which he immunized only one developed a fever (40° C. on the sixth day postpartum) and although the lochia revealed streptococci on culture the temperature dropped and the patient recovered. The blood culture was sterile.

In a second group of 200 pregnant women who were seen after the onset of labor for the first time, Louros injected 1 c.c. (500,000,000 bacteria) of the vaccine and 50 c.c. of an antistreptococcus serum. One woman died of typhus fever, another developed a fever of 40.2° C. on the fourth day postpartum which subsided, and a third woman had a fever of 39.6° C. on the seventh day postpartum which likewise dropped to normal. This investigator considered his good results to be on a sound basis and gave as proof the confirming results of serologic studies. The blood of the patients immunized showed no agglutination in 1 to 50 before injection and six days after immunization an agglutination titer of 1:800. Also, the bacteriotropine test showed a reaction between 1:100 and 1:350. He also employed the agglutination method of Koch and Kleine, and the method of Neufeld for the determination of bacteriotropines.

A control group of 333 women who were delivered by the same methods and technic were followed, and of this number 38 developed puerperal fever, 5 had streptococci in the blood, 10 had local streptococcal infections, and the remainder had putrid infections.

In 1923, at the French Congress on Puerperal Fever, both Brauha and Hauch presented evidence of the value of vaccines in the prophylaxis against puerperal fever.

Haertel, in 1925, utilized Louros' vaccine and method of immunization in the Athens Obstetrical Clinic. In 367 immunized parturients, only 3 developed endometritis and 2 had a fever although 80 operative deliveries were performed. The lochia of these 3 patients did not contain streptococci. In a control series consisting of 786 nonimmunized parturients, including 68 operative deliveries, 24 developed puerperal fever of which number 8 died. Seven of the fatal cases were due to streptococcal and one to staphylococcal infection. He reduced the mortality from 1.3 per cent to 0 and the morbidity from over 37.5 per cent to 3.26 per cent.

In the same year, Louros published more statistics on the active and passive immunization of pregnant women. Of 682, 483 received a simple dose of both serum and vaccine, while 199 received two doses of vaccine. Although 182 developed fever during the puerperium, only 18 had endometritis and none died of puerperal fever. He describes three cases in which the Ruge-Philipp virulence test showed a definite

absence of virulency of the vaginal streptococci in the blood of the immunized woman but the presence of virulency in strange blood. He believed that since the vaginal streptococci became avirulent in the blood after three to four days the immunity became active and this period of negative phase (three to four days) was overcome by the serum. Louros considered the patient protected against a blood infection but not against a local one, i.e., endometrial or parametrial.

It is evident from an analysis of the recent work that from the clinical standpoint vaccination of pregnant and parturient women against streptococcal infection is a valuable measure. The immunologic studies of two investigators, Jötten and Louros, demonstrate the presence of antibodies in the blood of the actively immunized women. However, it should be noted that proper control groups were not studied so that certain inconstant factors as seasonal variations, complications of pregnancy and labor, and individual technics were not eliminated. Furthermore, it is to be observed that all the investigators were careful to wash the streptococci several times before using them, thus eliminating all soluble bacterial products from the vaccine.

With the establishment of toxin production by the *Streptococcus hemolyticus* isolated from the blood of patients with puerperal fever, as reported in June, 1925, by Lash and Kaplan, immediate efforts were made to determine whether an antitoxin could be produced. The demonstration of antigenic properties of the toxin reported in April, 1926, made it possible to use this toxin in actively immunizing women against streptococcal infections. Therefore, it was the purpose of this study to determine whether the addition of toxin to the organisms increased the potency of the mixture utilized to immunize pregnant and puerperal women. Since previous workers have already demonstrated in determining the efficacy of the streptococcal vaccines that the immunologic and clinical curves run practically parallel, it was deemed unnecessary to follow both lines of study. The clinical method was chosen since in the final analysis the true value of any prophylactic or therapeutic measure must be used upon its effect on the patient, as determined by adequately large and accurate statistics. While this work was in progress, studies by Becker and Louros and Scheyer, in 1927 confirmed the early work of Lash and Kaplan on toxin production by puerperal fever *Streptococcus hemolyticus*. The confirmatory evidence was obtained by these investigators by studies with the toxin obtained from the *Streptococcus hemolyticus* from puerperal fever in lower animals demonstrating the antigenic properties of the toxin.

#### PREPARATION OF STREPTOCOCCAL TOXINS

Fourteen strains of hemolytic streptococci isolated from the blood of patients with puerperal fever which proved to be toxin producers were used. The organisms were grown in plain veal infusion broth (P<sub>H</sub> 7.4) for forty-eight hours, at 37.5° C., then heated to 55 or 60° C. for one hour. After shaking to break up the clumps of bacteria the organisms were counted. The toxins from these 14 strains were ob-

tained by growing the organisms for four to six days in the same broth as described above, at 37.5° C. The cultures were then passed through paper pulp and then through Berkefeld N filters. These toxins were found capable of producing an area of redness and swelling 1.0 cm. or more in diameter, in susceptible people when only 0.1 c.c. of a 1-1000 dilution of the toxins was injected intracutaneously. This amount of diluted soluble toxin was arbitrarily chosen as a skin test dose. One cubic centimeter of toxin mixture contained one billion streptococci in 1 c.c. of the undiluted toxins or 10,000 skin test doses. Thus the mixture contained the exotoxin and the endotoxins or toxic substance of the streptococcus. Two per cent sodium ricinoleate was added which according to the work of Larson and his associates based upon a study of scarlet fever and diphtheria toxins, prevents any general reaction.

#### METHOD OF CLINICAL USE OF STREPTOCOCCAL TOXINS

Unfortunately there is no accurate method to determine the susceptibility of a woman to streptococcal infections, for it is common knowledge that the normal spontaneously delivered woman may develop puerperal fever without apparent cause. The only acceptable method of evaluating the effect of active immunization is to inject in a large series every alternate case and to compare the results.

Frequently the only possible time for immunization was immediately after delivery as some women were not seen until the onset of labor. At first it was considered that the development of immunity in these cases might not occur before the onset of the disease, i.e., four to five days after delivery. In order to determine the optimum time for immunization a group of women were inoculated in the prenatal clinic within three or four weeks before the expected delivery and another group were given the toxins before (three to four weeks) and also immediately after delivery. A No. 22 needle, one and one-half inches long was used. All inoculations were given intramuscularly (left deltoid or left thigh muscles, by one individual). (A. F. L.)

#### REACTION TO STREPTOCOCCAL TOXINS

Within six to eight hours after the injection which was not painful, the area became tender, then red and swollen. In eighteen to twenty-four hours the area of inflammation measured from 4 to 8 cm. in diameter. This local reaction was more marked when some of the toxins escaped into the skin and subcutaneous tissues. After twenty-four hours the reaction began to subside and disappeared in thirty-six to forty-eight hours. Some tenderness remained for three to four days. In the 1689 injections given, an abscess developed in the arm of one patient and required hot fomentations, incision and drainage. No severe constitutional effects were noted.

To determine whether any constitutional reaction occurred, three series of patients were carefully observed for twenty-four hours for rises in temperature, pulse and leucocyte count. The three series consisted of (1) men, of (2) nonvaccinated puerperal women, and of (3) vaccinated puerperal women. The variation of the pulse, temperature, and leucocyte count in the group of men was negligible. In only one patient of the second group was there a rise in temperature which occurred on the first day of the puerperium due to an acute nasopharyngitis. The leucocyte counts dropped in the majority of the patients. The vaccinated puerperal women developed fever in 3 instances out of 10. There was an increase of only 1000 leucocytes the day following injection in two patients and a drop of as many in a third. In no case did the temperature rise above 102° F. or persist for more

than four to five days. It is not unlikely that the fever was produced by an intercurrent infection. The same, and in some instances, greater variations in the leucocyte counts occurred at twenty-four-hour intervals in both vaccinated and control puerperal women who were afebrile.

The same obstetricians delivered the control and the immunized women, thus avoiding the factor of variation in technic.

McKinley in a statistical study found a seasonal variation in the incidence of puerperal fever. In the series studied in this report, this element does not enter into consideration as the work extended throughout the year.

The influence of a negative phase, which according to Wright follows the injection of a vaccine, was disregarded in this work, because available evidence throws grave doubt upon its occurrence. For instance, Kolmer states in his textbook that most immunologists fail to recognize it. Moreover, were a negative phase to occur, the increased natural immunity found in puerperal women demonstrated by Colebrook and Fry, would tend to have a neutralizing effect. By the time the natural immunity begins to wane, the active immunity following the streptococcal toxins administration could be expected to appear, for Louros found that within six days after inoculation specific antibodies were formed. The opinions of Kolmer and Colebrook and Fry were borne out by my experience in immunizing a group of puerperal women within twenty-four hours after delivery. For in no case was there any clinical evidence of a negative phase occurring after the inoculation with the streptococcal toxins.

The earlier workers used 500,000,000 organisms and found a beneficial effect and no harm resulting. A larger dose was therefore considered in order to limit the immunization to one single injection. Preliminary observations were first made with  $\frac{1}{4}$ ,  $\frac{1}{2}$  and 1 c.c. of the toxins. As no general reaction resulted with the smaller doses and because 1 c.c. was used without harm the latter was chosen as the standard dose. The same precautions were observed as in the use of any vaccine or toxin. Only a single injection was made, consisting of 1 billion hemolytic streptococci and 10,000 skin test doses of toxin except in one group of women where two doses of toxins were given.

The control group consisted of 1216 delivered patients, 452 white and 738 negro women varying in ages from fourteen to forty-five years (67 per cent were sixteen to twenty-five years old). Of these, 441 were primiparae and 732 multiparae.

Group I included 1261 delivered mothers who were inoculated within twenty-four hours after delivery. There were 431 white and 830 negro women. Their ages ranged from twelve to forty-eight years, 67 per cent of them being from fifteen to twenty-five years old. Thirty-seven per cent were primiparae and the remainder multiparae.

Group II included 230 delivered women who received one injection of toxins within three to four weeks of delivery, and none after delivery. Sixty-six were white

and 164 negro women, whose ages ranged from seventeen to forty years of age, 75 per cent being between seventeen and twenty-five years. In this group 41 per cent were primiparae.

Group III comprised 198 delivered women, who were vaccinated three to four weeks before delivery and again within twenty-four hours after delivery. Sixty-nine were white and 129 negro women, their age variation being fifteen to forty years, with 65 per cent being between fifteen and twenty-five years.

An analysis of Tables I, II and III, where the incidence of the various predisposing factors to puerperal fever is given, furnishes the follow-

TABLE I. INCIDENCE OF PREVIOUS INFECTIOUS DISEASES

	CONTROL GROUP (1216 WOMEN)	GROUP I (1261 WOMEN)	GROUP II (230 WOMEN)	GROUP III (198 WOMEN)
Puerperal fever	85	86	8	13
Scarlet fever	97	87	21	15
Erysipelas	1	3	0	0
Rheumatic infection	4	11	2	0
Chorea	3	0	0	0
Sore throats	136	145	27	23
Gonorrhea	18	27	2	1
Influenza	30	89	29	18
Pneumonia	51	76	11	16
Typhoid	22	34	5	5
Malaria	18	18	5	3
Diphtheria	40	33	11	5
Syphilis	25	21	0	0

ing significant observations. It is of interest to note the relation between the occurrence of previous streptococcal and other infectious diseases and the incidence of puerperal fever. (Table I.) With the exception of scarlet fever, streptococcal infections confer only temporary immunity and in some individuals a decreased resistance to later infections is produced. (Kolmer.) As this study is chiefly concerned with the comparison of groups of inoculated individuals with a control group, detailed consideration of these various factors will not be made here. It is sufficient to note that there is very little difference in the incidence of the infectious diseases in these groups thereby paralleling the predisposing factors.

TABLE II. INTERVAL SINCE LAST COITUS

	DAYS						WEEKS			MONTHS								
	1	2	3	4	5	6	1	2	3	1	2	3	4	5	6	7	8	9
Control Group	19	43	16	11	5	1	143	129	83	194	129	86	45	36	30	22	35	66
Group I	27	45	15	12	4	2	147	147	76	207	186	104	62	29	25	35	75	29
Group II	3	6	3	4	2	3	24	21	26	24	33	24	12	5	5	1	3	14
Group III	3	5	3	0	2	0	22	21	20	30	30	15	8	9	5	3	4	8

As to the incidence of the time interval since the last coitus, it is observed in Table II that there are no marked differences in the various groups. The incidence of recent coitus is far greater than the incidence



of morbidity or mortality due to puerperal fever. However, more detailed analysis of these statistics will be considered later.

Finally, the most important predisposing factor in the occurrence of infection is the labor. In comparing the statistics of the groups (Table III), the incidence of long labors and operations is about the same. Therefore, the various conditions enumerated above, the parallel percentage of the incidence of the usual predisposing factors to puerperal fever and the standard dose of toxins used for the vaccinations, make these statistics lend themselves to proper comparison and allow conclusions to be drawn from the results.

TABLE III. DURATION AND CHARACTER OF LABORS AND DELIVERIES

	CONTROL GROUP	GROUP I	GROUP II	GROUP III
<i>Duration in hours</i>				
1-5	170	199	46	18
6-10	258	318	45	51
11-15	222	209	39	34
16-20	108	105	25	18
21-25	86	70	17	18
26-30	50	37	8	8
31-35	24	14	3	5
36-40	19	26	4	2
41-45	7	6	0	3
46-50	9	4	2	3
51-55	5	4	1	1
56-60	3	2		
61-65				
<i>Operations</i>				
Repair of perineal lacerations, first	137	174	32	27
second	26	41	5	2
third	2	0	0	0
Episiotomies	175	155	26	26
Low forceps	24	32	3	5
Midforceps	27	14	3	2
High forceps	3	4	0	0
Version and extraction	4	6	0	1
Manual removal of placenta				
Uterine packing	3	4	2	0
Manual dilatation of cervix	6	2	0	1
Bag induction	2	0	1	0
Dührssen's incisions	1	1	3	0
Curettage	1	3	1	0
Craniotomy	1	0	0	0
Repair of cervical lacerations	0	2	0	1
	0	4	0	0

The results determined by comparing the incidence of the morbidity and mortality of the various groups are shown in Table IV. Patients having a temperature of 100.4° F. or over between the second and tenth day postpartum were classified under morbidity. The puerperal fever group included those patients with continuous fever for at least four to five days with pain in the lower abdomen, and tenderness over the uterus and broad ligaments and presence or absence of lochial changes.

It is observed that the incidence of morbidity is about the same in all the groups. This observation raises the question whether these temporary rises in temperature are due to true infections of the uterus. In all these patients there were no localizing symptoms referable to the pelvic viscera. It is, however, probable that a mild endometritis may be present without clinical local symptoms, therefore allowing for a certain number of the fevers in the puerperal women to be due to mild uterine infections. But other causes may give the same clinical picture, such as absorption from temporary lochiometra, mild pyelitis, upper respiratory infections or breast engorgement or infection. Although there were only four positive smears for gonococci, it is probable that the incidence of latent gonorrhea is much higher. The best means for determining the presence of morbidity would be the finding of inflammatory residuum in the pelvis if the fever remained for several days. It is conceivable that mild endometritis may subside and leave no determinable evidence of an infection.

TABLE IV. INCIDENCE OF MORBIDITY AND MORTALITY

	NO. OF PATIENTS	MORBIDITY PER CENT	*PUERPERAL FEVER PER CENT	MORTALITY PER CENT
Control Group	1216	226-18.6	34-2.8	0
Group I	1261	245-19.4	11-0.87	0
Group II	230	44-19.0	2-0.86	1-0.43
				(Pulmonary embolism)
Group III	198	42-21.2	1-0.51	0

\*See text for the distinction between puerperal fever and morbidity.

Another explanation for the lack of variation in incidence of morbidity in the different groups may be that the immunity acquired by vaccination with toxins is general rather than local. Also the fevers occurring in Group I may be attributed to the reaction of the vaccination although the experimental groups did not certainly demonstrate this.

That vaccination with toxins is beneficial can be deduced from the definite marked variation in the incidence of puerperal fever in the control and in the vaccinated group. Thus the 2.8 per cent incidence found in the 1216 control patients is reduced to 0.87 per cent in the 1261 vaccinated puerperal women, to 0.8 per cent in the 230 vaccinated pregnant women receiving one dose and to 0.51 per cent in the 198 vaccinated puerperal women who received two doses. Puerperal fever may result from various bacteria but the streptococcus is the commonest and most feared. This fact has been again emphasized recently by Harris and Brown at Johns Hopkins Hospital where in 168 uterine cultures of puerperal fever women, in 113 or 67 per cent streptococci were found alone or in association with other organisms.

It is of further interest to determine the most frequent etiologic factors in the cases of puerperal fever that occurred in these series.

For preventive medicine is indeed of great importance in obstetrics since the achievements of prophylaxis have by far outdistanced those of therapeutics.

In the control group, of the 34 patients with puerperal fever, although no age was exempt, 27 or 79 per cent were under twenty-five years. This high incidence of young women is of no or only slight significance as 69 per cent of the census of the wards was below twenty-five years of age.

The negro women predominated in the ratio of 2.4 to 1. The ratio of colored to white women was 1.63 to 1.0 in the total group, therefore, the difference in the incidence of puerperal fever in the two races cannot be explained on this basis (i.e., ward census). Harris and Brown in their study of puerperal fever statistics found that streptococcal puerperal infection occurred approximately three times more often in the blacks than in the whites, although the two races are approximately equally represented in their wards. They also quoted from some unpublished statistics of J. Whitridge Williams, who found that in the last 5000 deliveries in the Johns Hopkins Hospital, ending November 1, 1927, the incidence of puerperal infection was approximately twice as great among the blacks as among the whites. Harris and Brown attribute this difference in incidence in the races to defective hygienic conditions, poor physical conditions and liability to infections of all kinds. They think that immunity and resistance are not so well developed in the black as in the white race. Kolmer states that well-marked examples of racial immunity are extremely rare although it is believed that negroes are immune to yellow fever and Mongolians to scarlet fever. One may also consider that the patients in this study come from that strata of society where there is only a survival of the fittest. Moreover, it is fair to assume that these individuals who have survived to womanhood have run the gauntlet of the many infections present in their environment and have developed an immunity. Therefore, another etiologic factor alone or in conjunction with that of race susceptibilities or with another factor should be sought.

Primiparae were predominant, and when their number is combined with secundiparae, there is the same incidence as the age period, that is, under twenty-five years of age, or 79 per cent. Although in multiparous women, the local physical defense mechanism is broken, which consists of intact pelvic floor, closed vaginal orifice, normal vaginal flora and closed cervix, yet less trauma occurs to the local tissues for delivery to take place in them than in primiparous.

As to the other factors in the etiology of puerperal fever, one finds that its incidence in the histories of the patients is 8.8 per cent compared to 6.9 per cent in the whole group. Scarlet fever occurred in 8.8 per cent as compared to 7.9 per cent in the complete group. Common sore throats were present in 14.7 per cent as compared to 11.1 per cent

in the total group. A history of gonorrhea or positive smears for gonococci in the present pregnancy had an incidence of 11.7 per cent while in the whole group the incidence was 1.5 per cent. The Wassermann reactions of the puerperal fever patients were negative.

Coitus has always been considered a very important predisposing etiologic factor for puerperal fever. In this series of puerperal infections, 2 patients had coitus two days, 2 one week, 2 two weeks, 3 three weeks, and 22 or 64.7 per cent from one to nine months before delivery.

As to the character of labor in the puerperal fever of the control group, it is found that 26.4 per cent were operative while in the whole group, 6.7 per cent were operative. The difference in the two series is marked.

#### GROUP I

In this series, puerperal fever occurred in 10 black women and in only 1 white. The age and parity relationship was about the same as in the control group, that is, the majority of the patients were under twenty-five years of age and were either primiparae or secundiparae. Only one patient gave a history of repeated sore throat.

One patient gave a history of coitus three days before delivery, three one week before delivery, one three weeks, and five from two to nine months before delivery. Eight of the labors terminated spontaneously and three operatively.

One death occurred in the entire series of 2905 patients. This patient was in Group II, having received 1 c.c. of toxins one month before delivery. She was a colored woman, twenty years of age, who delivered her first child spontaneously without laceration after a labor of fifty hours and twenty minutes. No vaginal examinations were made. She had no previous infectious diseases. Coitus occurred one week before delivery. Cultures of the cervix postpartum revealed *B. coli* in aerobic cultures and nonhemolytic streptococci in anaerobic cultures. The blood culture was sterile. She ran a moderately septic course from the fifth to the twelfth day postpartum, apparently having an acute metritis and parametritis. A rectal examination was performed to determine the extent of the parametritis. Following this examination, the pulse and respirations became rapid, the patient developed a cold sweat and cyanosis. She died twenty-four hours later with the clinical symptoms and signs of embolism. Permission for autopsy was refused.

#### SUMMARY AND COMMENT

This investigation to determine the value of vaccination with toxins in pregnant and puerperal women as a prophylaxis against streptococcal puerperal fever was based on the clinical and immunologic evidence of other investigators that some beneficial effect is derived from the use of streptococcal vaccines. Inasmuch as it is established that the toxin produced by the *Streptococcus hemolyticus* obtained from puer-

peral fever patients has antigenic properties, it was added to the vaccine. The resulting mixture contained, therefore, all the streptococcus toxins. The series of patients used in this study presented such parallel incidence as to the various etiologic factors of puerperal fever that, with a standard dose of toxins, they could justifiably be utilized for comparative studies. The effect of the vaccination with toxins was expressed in the incidence of morbidity and mortality. The other variables as seasonal, technic of the obstetrician and the vaccinator were recognized and given due consideration in controlling the work.

The significance of the classification of morbidity is questionable because the presence of an ephemeral fever in the puerperium can hardly be considered as evidence of pelvic pathology in all patients. Morbidity in the puerperium should be classified on the basis of morbid changes occurring in the generative tract as judged by the clinical course and bacteriologic findings. At times, it is realized that this would be difficult in the absence of definite localizing symptoms. In such instances, the diagnosis would have to be made by the elimination of simulating conditions. Therefore, puerperal fever as indicated by acute endometritis and its associated pathology which either heals or leaves definite inflammatory changes in the pelvis and does not cause death would correctly be considered under morbidity. It is for these reasons that Table IV has the statistics under morbidity and puerperal fever.

A temporary fever with no other symptoms or findings may indicate a reaction of the organism to an invasion by a foreign body or bacteria, without the invader gaining a foothold and without morbid changes being produced. Thus, patient R. G. illustrates this statement. She was a Mexican woman, twenty-four years of age, who had had six pregnancies. Following the delivery of one of her children she developed puerperal fever which lasted for two months. The present delivery occurred spontaneously after twenty-four and one-half hours' labor. She received her toxins vaccination within twenty-four hours after delivery (i.e., Group I). On the third day postpartum her temperature rose to 103° C., pulse 96, and she had a headache and a chill. The fever remained for thirty-six hours and then subsided in a few hours. In the cervical culture was isolated a pure growth of *Streptococcus hemolyticus*. There was no tenderness over the corpus or broad ligaments and no visible change in the lochia. It may be properly assumed that this febrile reaction was a definite defense reaction of the body induced by the toxins vaccination against the invasion of the *Streptococcus hemolyticus* isolated from the cervix and uterine secretions. This one case is suggestive but not conclusive as many more such instances would be necessary to be convincing.

Among the various predisposing factors in the development of puerperal fever, the negro race and operative deliveries predominate over the other factors as age, parity, and coitus. A difference in the immunity mechanism in the negro and white races presumed by Harris and Brown finds support in the results of the present study. In Group I 10 of the 11 patients who developed puerperal fever were colored. This fact would seem to indicate a difference in their power to acquire immunity as well as difference in their natural immunity as demonstrated in the control group. Another explanation of this racial variation is the high incidence of gonorrheal infections in the negro race. Although the incidence of positive vaginal smears is low among the negro women of this study, our experience has been that it is very difficult to get positive smears in spite of the presence of the gonococci. It is not an uncommon experience to find that before delivery the smear is negative for gonococci and after delivery either the baby develops an eye infection or the mother runs a low grade puerperal septic course which calls the attention again to the generative tract. At this time the smears will show many gonococci. The presence of a gonorrheal endocervicitis predisposes toward upper genital infections during labor as well as during menses since other organisms are invariably plentiful and usually follow the gonococci.

Operative deliveries are unequivocally a great factor in the production of puerperal fever. This fact is such common knowledge that the above observations merely confirm it. The reasons are quite evident. Resistance to infection is dependent upon the intactness of the epithelial lining and upon the normality of epithelial cells. Therefore, the injury to or destruction of these elements can well explain the deficient local defense mechanism. There seems to be a false notion that if the operator wears sterile gloves and gown, he may invade the generative tract and at the same time forget about traumatism and the ever-lurking bacteria in the vagina or on the vulva.

Another important factor in streptococcal infections is the streptococcus carrier in the medical or nursing personnel. The recent report of Watson and his coworkers has demonstrated the importance of this factor in the production of an epidemic of puerperal fever. After a careful bacteriologic study, this was the only demonstrable factor.

#### CONCLUSIONS

In the development of puerperal fever there are many unmeasurable factors such as virulence of the bacteria, the local resistance and the constitutional immunity of the patient which play varied rôles in preventing or permitting the disease to occur. However, on the basis of the evidence brought forth by the above controlled study, one is led to conclude that:

1. The use of a streptococcal vaccine has some value toward lowering the incidence of morbidity and mortality in puerperal fever as determined by immunologic and clinical evidence offered by German investigators.

2. The toxic filtrate of hemolytic streptococci from puerperal fever has antigenic properties as demonstrated by the work of Lash and Kaplan, and confirmed by the studies of Becker, Louros and Scheyer.

3. The fact that among 1216 puerperal women there was an incidence of 2.8 per cent of puerperal fever and among 1261 puerperal women vaccinated with streptococcal toxins only an incidence of 0.87 per cent in the presence of parallel variables would indicate the value of vaccination with the toxins as a prophylactic measure against puerperal fever.

4. There was no evidence of a negative phase after inoculation with streptococcal toxins.

5. The lowest incidence of puerperal fever was in the group in which toxins were administered before and after delivery, that is, 0.51 per cent (Group III). This suggests the added advantage of two doses of toxins, one being given three to four weeks before and one immediately after delivery.

6. The negro women have puerperal fever more frequently than the white. This may be explained by the inferior immunologic mechanism of and the higher incidence of gonorrheal infections in the colored.

7. Operative deliveries are more often followed by puerperal fever than spontaneous ones.

8. Since it is not feasible nor necessary to immunize every expectant mother, it is suggested that the pregnant negro women and all pregnant women with probable operative deliveries or with frequent streptococcal infections elsewhere in the body should receive vaccination with streptococcal toxins.

9. Further work should be carried out using multiple doses of toxins in large series of properly controlled cases.

NOTE: I wish to acknowledge the help given me by W. A. Jamieson, Director of Biological Laboratories of Eli Lilly and Company, who was responsible for the frequent allotments of fresh toxins and bacterial suspensions prepared from my strains of puerperal fever streptococci.

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## THE PRESENT STATUS OF CESAREAN SECTION WITH PARTICULAR REFERENCE TO ITS EMPLOYMENT IN ECLAMPSIA\*

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CESAREAN section can no longer be regarded as a dramatic and tragic procedure, used as a last resort and performed for the greater part on women exhausted from prolonged labor or attempts at delivery. The latter in themselves constituted an additional factor in the excessive mortality which formerly prevailed. The advent of safety has extended gradually and progressively its use for a wide diversity of indications, and these include many pathologic conditions in themselves dangerous to life. It is therefore significant that with these adverse factors a maternal mortality of less than 1 per cent and a fetal mortality of less than 2 per cent is reported by specialists in the larger clinics. In competent hands, the surgical mortality is comparatively negligible. Some have reported from 90 to 100 consecutive cases without a maternal death, and in one instance 145 were reported with one maternal and two fetal deaths. The investigations in two of our larger cities, one north and one south, have shown a wide disparity in the general results obtained, as compared with the experiences of individual operators. In these cities, the maternal mortality was found to be 10 per cent plus, and the fetal mortality 10 per cent. The eclamptic cases reached an unexpected peak of 42.7 per cent mortality, resulting in an especial warning against cesarean section in eclampsia. It appears that those making this survey were so impressed by these adverse findings that in the warning accompanying this report against indiscriminate cesarean section, they still further magnified the operative danger by comparing it with the medical treatment of eclampsia, citing a mortality of less than 5 per cent. As a matter of fact, the average maternal mortality is from 7 to 10 per cent and the fetal mortality from 15 to 20 per cent under nonoperative treatment. A few

\*Read at a meeting of the Alabama State Medical Association, Mobile, Ala., April 18, 1929.



highly skilled obstetricians have reported a maternal mortality of 5 per cent; one series of selected cases coming under treatment early gave a mortality of 1.7 per cent in the medical treatment of eclampsia. As a result of these investigations, the occasional and average operator was especially warned against doing cesarean section, except where delivery by the vaginal route was impossible, not even permitting it to be done where prompt delivery is a requisite for the safety of the mother. More especially is this mandatory when the child is premature or the death of the fetus has occurred in utero. With limits like these placed on the average operator, the surgical mortality rate in his hands will be from 10 to 20 times higher than those of the skilled specialist, because he will only operate on those whose delivery has been attempted, or who have been infected, or who have passed through an unavailing course of medical treatment, or whose vitality is spent, and for whom small hope is left. The obstetric results will also suffer, as both maternal and fetal mortalities will ascend as a result of podalic versions, high forceps deliveries, and embryotomies. Hence there is an open question to be settled, to accomplish which there must come reports from the average surgeon of his work, the indications followed, the results obtained in maternal and fetal mortalities, and finally from follow-ups of the maternal and the fetal morbidity.

Parturition injuries to the pelvic floor and birth palsies are avoided by cesarean section, and maternal and fetal morbidity reduced. In the service of F. G. DuBose and D. H. Doherty at the Vaughan Memorial Hospital and Burwell Infirmary, during the past fourteen years, there have been one hundred consecutive cesarean sections, which have been taken from the records for this report. The indications are detailed in the order of frequency. The foremost includes eclampsia, placental toxemia, nephritis of pregnancy and persistent hyperemesis gravidarum, and may be grouped under nephritis or toxemia of pregnancy. The next group wherein cesarean section is used as a substitute for podalic version or high forceps delivery, includes placenta previa, premature separation of the placenta, massive uterine hemorrhage before the onset of labor from any cause, the senile uterus, elderly primipara, excessive hypertension, and transverse presentation. The third group includes obstruction of the pelvic outlet from deformed or contracted pelvis, uterine or ovarian tumors, cervical or vaginal atresia, malignant disease of the cervix, vagina, or vulva, and excessive adiposis. The fourth, previous cesarean section.

In addition to these, which we have followed, advanced pulmonary tuberculosis and pulmonary edema also are classed among indications by other writers.

*Contraindications.*—There is almost a uniform agreement among writers that the classic cesarean section is only safe in selective cases. It is to be avoided after the onset of labor; the rupture of membranes,

the attempts at forceps delivery; and more especially after the incidence of infection, as septicemia or peritonitis is an outstanding danger. These contraindications are stressed with an emphasis the validity of which is not borne out by the results in our own clinical operative experience. The frankly infected uteri previous to operation, in our observation, have a better chance following the Porro operation than they have under the medical or the expectant plan of treatment, even though parturition has been accomplished without section in those who were infected previous to or at the time of delivery. Some of these have been saved in our hands, though apparently hopeless, by supravaginal amputation of the uterus, and drainage. Temporary exteriorization of the uterus, especially in the young, where the Porro operation would be a tragedy, has been done with an exceedingly low mortality. The conservation of the uterus in young women with the possibility of future pregnancy recommends it for serious consideration. After delivery by section, the sutured uterus is left on the abdomen, the abdominal wound being closed around it until sepsis has subsided and involution has taken place. It is then replaced within the pelvic cavity.

*Technic.*—Except in the urgent emergencies, such as hemorrhage or eclampsia, prior to operation the patient should be given a purgative enema; the lower abdomen and vulva shaved and thoroughly cleansed with soap and water; a vaginal douche given, and a 1 per cent mercurochrome solution instilled into the vagina; the bladder emptied voluntarily, or by catheter if necessary, immediately before going to the operating room; thorough infiltration of the abdominal wall with  $\frac{1}{4}$  of 1 per cent apothesine solution where the incision is to be made, following the suggestion of Williams, from 5 to 7 inches in length,  $\frac{3}{8}$  below and  $\frac{1}{8}$  above the umbilicus. After incising the abdominal wall at this point, a small retractor holds the wound open and the parietal peritoneum is anesthetized by injecting, with a long needle, the apothesine solution over an area of 6 to 8 inches from the abdominal incision on both sides. The hand can then be passed between the uterus and abdominal wall without pain to the patient, and the uterus delivered through the incision. If one rotates the uterus laterally, delivers one cornu, then the fundus, and then the other cornu, a smaller incision can be used in the abdominal wall. As soon as it is delivered on the abdomen, the broad ligaments are grasped on either side firmly by an assistant, enabling him to completely control hemorrhage by manual pressure. This grasp is continuous throughout the incision of the uterus, the delivery of the child and placenta, and the final suture of the uterine wound. As soon as the assistant has grasped the delivered uterus as above described, if the abdominal wound is a very long one, it is held together by tenaculum forceps close to the uterus, to prevent intestinal eventration or contamination of the abdominal cavity. One or two gauze rolls are placed above the uterus over the incision, and one long roll is wrapped around the uterus underneath, the assistant's hand grasping it, as an additional precaution against soiling or contaminating the abdominal cavity. An incision about 3 inches in length is made anteriorly in the body of the uterus in the midline, the upper end of which reaches the fundus. With two fingers, this incision is enlarged approximately to 5 inches; the membrane is ruptured, and the child and placenta are delivered and handed to the nurse. As soon as the child cries, the cord is clamped and cut. All shreds

of membrane are carefully removed from the uterine cavity, which is then swabbed with a gauze sponge saturated with 1 per cent mercurochrome solution. The uterine wound is closed in layers. First, a running stitch of plain No. 2 catgut approximating the endometrium; a second running or interrupted mattress suture of No. 2 chromic catgut is placed immediately above this approximating myometrium. A seromuscular running lock stitch of No. 2 chromic catgut closes, and as a rule, completes the suture of the uterine wound. Rarely a few supplementary sutures are necessary to complete the invagination of the serosa. If the uterus becomes flaccid, or shows a tendency to ineffectual contraction while it is being sutured, or at any time before its return to the pelvic cavity, 1 c.c. of pituitrin is injected into the myometrium; to further avoid uterine hemorrhage, a hypodermic of ergot is given before the patient leaves the table. In the high blood pressure, eclamptic, or extremely toxic cases, the uterus is permitted to bleed in order to reduce the pressure and to remove toxic material. A compensatory amount of a 15 per cent glucose and physiologic salt solution is given, from 400 c.c. up to 1000 c.c. as indicated. After removing the gauze rolls from the abdominal wound, it is rarely necessary to mop out blood from the peritoneal cavity as none has entered it. The uterus is dropped back in the pelvic cavity, the omentum is spread over the fundus without traction, and the abdominal wound is closed in layers with catgut up to the skin. Three or four figure-of-eight tension sutures of colloidal linen or silk reinforce the aponeurotic approximation with the lower loop, and take the tension off the skin sutures with the upper loop. The skin is closed usually with non-absorbable colloidal linen in a running stitch, less frequently with an interrupted suture.

The results of this technic have been so satisfactory that the vaginal transperitoneal, the extraperitoneal, and the intraperitoneal-retrovesical cesarean section have not been considered. Nor have we done the transverse incision in the cervix or in the fundus in opening the uterus. The variations from the classic cesarean section just mentioned we commend only to those whose superior surgical skill from an unusually enormous volume of cesarean operations admits of such a versatility in varying the technic. The consideration of the average operator, who does approximately one cesarean section each month, is to perfect himself in one operative technic and adhere to it consistently. In the most of these cases, particularly in the eclamptic and hemorrhagic types, speed is especially essential, and rapidity of operating is not consistent with an unfamiliar and unpracticed technic. From the beginning of the incision in the abdomen until the closure of the uterine wound after the delivery of the child, five or ten minutes is all that is necessary. To close the long abdominal incision in layers with careful coaptation of each layer, ten or twenty minutes are needed.

In the very toxic cases, gastric lavage is done and, following complete emptying of the stomach, from 2 to 6 ounces of magnesium sulphate are given by gavage. As soon as the patient is returned to bed, magnesium sulphate clysters consisting of 3 ounces of a saturated solution are introduced every two hours until liquid stools are obtained through the

rectal tube, or the bowels begin to move freely. Where this laxative effect is delayed, a hypodermic of peristaltin and pituitrin is given as an aid to the above measures.

#### REPORT OF CASES

This report includes one hundred consecutive cesarean sections since 1915. In these, there have been since 1925, 45 without a maternal death. Local anesthesia was employed in almost every one of these cases. In the previous 55 cases, there were two maternal deaths. There were no fetal deaths where the operation was done after the seventh month of gestation, except where intrauterine death has occurred previous to the operation. One infant just passed the sixth month, weighing two pounds when delivered, survived; and one delivered from a dying eclamptic woman in the early part of the seventh month, weighing four pounds, survived. Over two-thirds of the cases in this series were operated upon because of the toxemia or nephritis of pregnancy, enumerated under the first group of indications, one-half of which had eclampsia. In this group, there were two maternal deaths; one moribund at the time of operation, the other from a cerebral apoplectic stroke four days postoperative.

The next largest number was for placenta previa. Five per cent of the entire group had previous cesarean sections; 3 per cent were elderly primiparas, and 3 per cent were for deformities of the pelvic outlet. One or more came under the several indications outlined above; among these was a dwarf, 51 inches tall, weighing 60 pounds (baby weighed 4½ pounds, 18 inches tall; both survived); another with a ventral hernia and anemia, having a red count of 2,000,000 cells, a young primipara; following the cesarean section, the ventral hernia was repaired during the closure of the operative wound, both mother and child surviving without incident. One was an obese negress, sent to the hospital after forty-eight hours of ineffectual effort on the part of the midwife and doctor to reduce a prolapsed arm in a shoulder presentation, and do a podalic version. On admission the swollen and ecchymotic arm of a dead fetus was protruding from the vagina, the uterus was in tonic contraction and the woman exhausted. Under deep ether narcosis, there was no relaxation of the uterus, and cesarean section was done instead of embryotomy. The recovery of the woman was less eventful than was anticipated. One patient elected this method of delivery, and was supported in her choice by her husband and parents, and only because of their urgent insistence was it done. It is found from case reports in literature, that contracted pelvis first, placenta previa next, and pelvic neoplasm third, is the order of frequency for which the operation has been done.

## SUMMARY

In this series, eclampsia and allied toxic state represent over 60 per cent of the causes for which cesarean section was done, with practically no operative mortality, as the 2 fatal cases in this series in reality were not postoperative deaths. It is hard to understand why the mortality of cesarean sections done for the relief of eclampsia should give a mortality of 42 per cent, set forth in one recent survey, as these presented here, for the greater part were referred ones coming into the hospital from 20 to 100 miles away after the onset of the convulsions. Some were infected, some had attempts at forceps delivery, and all of them had been examined by either a physician or midwife many hours before admission to the hospital, and were neither early nor favorable cases.

It is significant that so small a number in this group had pelvic deformities, which speaks well for the absence of rickets in the rural South.

A decade ending in 1905 in my experience with eclampsia, treated nonsurgically, according to the then prevalent methods of elimination, morphine and veratrum, podalic version, high forceps delivery, gave a mortality rate of approximately 10 per cent. Under medical or surgical treatment, relatively equal or competent, the surgical results will greatly surpass the medical.

The average maternal mortality from all obstetric causes during 1925 in six southern states was approximately  $\frac{1}{2}$  of 1 per cent (0.478).

*Detailed Report of the Two Fatalities:*

CASE 1.—Aged thirty-nine years, white. Eclamptic, admitted in profound coma, following eclampsia of two days' duration. Catheterized specimen showed 4-plus albumin, 4-plus casts. Taken to operating room immediately, and under local anesthesia a 4 pound living girl was delivered. The coma deepened, and she died the same afternoon. The child is living. This woman was moribund when she was operated upon, and the living child is the only justification for operating on an extreme subject.

CASE 2.—Aged thirty-five years, white, para iii. Was admitted from another hospital with the following history: Six months pregnant. She was perfectly well until she had influenza ten weeks ago. She has been in bed during the past five weeks, with nausea and vomiting, a daily temperature varying from 99 to 102. For the last two weeks she has been in hospital with persistent nausea and vomiting, terrific morning headache. Tonsils removed one week before admission to this hospital. Patient extremely weak, sallow complexion, circles under eyes; throat shows evidence of recent tonsillectomy, not completely healed, and tongue quite coated. Lungs negative. Pulse rate 110. Heart enlarged two fingers to left, loud systolic blow at apex, transmitted to left. Tender over right kidney and gall bladder. Fundus of uterus just below the level of the umbilicus. Pelvic examination negative except for pregnant uterus.

Urine: Brown in color, acid, gravity 1022, albumin + + +, with quantities of casts.

Blood count: 2,600,000 red cells, 9,000 white cells, 82 per cent polymorphonuclears, 12 small mononuclears, 6 large mononuclears, 65 per cent hemoglobin. Diagnosis:

Toxemia of pregnancy with nephritis. She was kept under observation and treatment for four days, during which time her temperature ranged from 96.4 to 102. On account of the persistent nausea and headache, cesarean section was advised, which was done under ether anesthesia the fourth day after admission. Her postoperative condition was entirely satisfactory until the third day, when she died suddenly from cerebral embolism.

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## REPORT OF AN EXPLOSION OF ETHYLENE GAS RESULTING IN THE DEATH OF A MATERNITY PATIENT AND HER CHILD\*

BY REUBEN PETERSON, M.D., ANN ARBOR, MICH.

IT IS not surprising that fatalities resulting from explosions of various gases used to produce anesthesia should be unreported. No matter how honest he may be, the surgeon refrains from reporting the case, at least immediately, out of regard for the hospital in which the accident occurred. Sudden anesthetic deaths from chloroform and ether have been exploited in the press so long and frequently that such items have ceased to be news. Deaths, however, resulting from explosions of gases used in anesthesia are seized upon by the press and heralded from coast to coast. One only has to be unfortunate enough to be involved in such an accident to realize its sensational features. Letters of inquiry, even telegrams, pour in upon one, many of them phrased in such a manner as to show that the details of the accident have been grossly exaggerated. It is a bad time for the hospital and the surgeon, and neither one is anxious to publish details of the accident.

Again, the surgeon no longer feels competent to pass judgment on defects of anesthesia, so complicated have become the machines of its administration, complicated, that is, for the men whose experience was limited to the open method of giving chloroform or ether. Formerly, having had experience as an anesthetizer in many hundreds of cases, with or without justification, he felt himself quite an expert anesthetizer, and when he began to operate, he had his mind on the anesthetic as well as on the operation. Now all this to an extent has passed. Anesthesia is in the hands of specialists, and the surgeon must depend upon them. When a gas explosion anesthetic accident occurs, he hesitates to report it because he is not quite sure of his ground.

Whatever may be the explanation, the fact remains that there are relatively few detailed reports of deaths from gas explosions during anesthesia. It is to remedy this at least by the report of one case that I have complied with the request of numerous medical friends to give the details of an explosion in the maternity ward of the University of

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Michigan Hospital during the administration of ethylene which unfortunately resulted in the death of mother and child.

The patient was an unmarried girl of sixteen, mentally deficient, first pregnancy, who at 9:40 P.M., November 30, 1927, was well advanced in the second stage of labor. Owing to the strength and frequency of the pains and on account of the marked bulging, ether in slight amounts was given the patient until the arrival of a regular hospital anesthetist who took charge of the ethylene-oxygen anesthesia which for some months had been employed as an analgesic for the maternity patients.

The mixture employed in a McKesson apparatus was ethylene and oxygen, 25 per cent of the former and 75 per cent of the latter. The practice has prevailed with maternity patients to ask them to breathe deeply three times at the beginning of a pain. The mask is then removed from the face and the patient urged to bear down. In the latter part of the second stage when the head is extended over the perineum, it is customary to increase the amount of ethylene and decrease the proportion of oxygen until practically complete anesthesia is produced.

It is essential to keep in mind this technic of administering the ethylene since, as will be shown later, it had a distinct bearing upon the cause of the explosion which occurred after the fourth or fifth administration of the mixture before the proportions of the ethylene and oxygen had been changed.

The explosion occurred at approximately 10:10 P.M. It was violent and loud enough to be heard throughout the four-storied maternity building. The anesthetist was partly blown from her chair but fortunately escaped serious injury. The gas machine was seen to be on fire, but the flames were promptly extinguished by means of a blanket.

Immediately following the explosion the patient cried out and attempted to rise up to sitting posture on the delivery table. After resuming the recumbent position she went into opisthotonus, began coughing up large quantities of foamy blood, and became unconscious.

I was called immediately and arrived in the delivery room within ten minutes after the accident. The table was lowered in the Trendelenburg position to facilitate the emptying from the throat and mouth of constantly increasing amounts of blood. Finally a tracheotomy was performed in the vain hope it might be of some avail. The postmortem findings revealed why nothing could be done to save the patient. Almost immediately after the accident the patient's neck and face became greatly swollen and distorted by a marked emphysema. The heartbeat was at first fairly strong but gradually became weaker until death at 11 P.M.

At the time of the explosion crowning was taking place and the baby would have been born within a few minutes. After the accident the fetal head receded within the greatly relaxed introitus. The fetal heart could not be heard, any possible sounds, however, being obscured

by the patient's noisy respirations. Although it was thought improbable that the fetus was alive, it was deemed advisable to extract it on a chance it might be saved. Forceps were applied one-half hour after the accident and the child easily delivered by slight traction owing to the excessive relaxation present. The fetus showed no signs of life and all attempts at resuscitation were unavailing.

Dr. A. S. Warthin's autopsy findings were as follows: traumatic death, ethylene explosion during anesthesia for childbirth, multiple lacerations of lower trachea, great bronchi and parenchyma of lungs; massive hemorrhages throughout the lungs; interstitial emphysema of upper half of body; fatty degenerative infiltration of liver; subepicardial fatty infiltration with moderate right-sided cardiac dilatation; lipoidosis of adrenals; puerperal changes in uterus with laceration of the cervix; tracheotomy wounds; acute passive congestion of all organs; edema of meninges and brain.

At an investigation of the cause of the explosion made by the committee on anesthesia of the University Hospital assisted by Dr. E. J. McKesson of Toledo, Ohio, Professor Williams of the department of physics of the University of Michigan and Professor C. C. Meloche of the department of chemistry, on December 13, 1927, the following facts were elicited:

1. The rubber pneumatic face cushion was missing, but there were the remains of the celluloid hood under the collar which normally holds it in attachment to the metal parts of the face inhaler.

2. The breathing tube four feet long with a coil of wire running through from one end to the other showed three definitely punched out places where the rubber had previously been in continuity where the explosion had blown out the rubber between the coils of wire, leaving the wire exposed but apparently intact from one end to the other.

3. On top of the head of the mixing valve, the glass window, a circular window of about an inch and a quarter in diameter, had been blown out. The fine glass from this window was thrown to the ceiling by the force of the explosion,

4. The bottom of the rebreathing chamber was blown out together with the rubber glove fastened to this part of the chamber and used for rebreathing purposes.

5. In the breathing tube, a streak within the lumen of the tube about one-sixteenth of an inch wide seemed to travel from one end to the other. This streak looked like charred rubber for it was dark brown in color, and the texture of the rubber at that point was as hard as rubber which has been charred by coming in contact with a high temperature, looks and feels.

Since the explosion and its fatal ending, no ethylene has been used in the department of obstetrics and gynecology. In fact it has been



discontinued throughout the hospital, although its advantages had been appreciated through its employment in nearly 15,000 cases. While I do not favor its use in obstetrics for reasons which will be set forth later and while its disadvantages in regard to nonrelaxation in pelvic and upper abdominal surgery are many, there still remain many cases where it would be the anesthetic of choice because of the prompt recovery of the patient in comparison with ether. Why then should its use be abandoned because of a fatal accident when we know that many patients in the past have succumbed from ether improperly administered? Obviously the answer must lie in the causes of the explosion and whether these can be eliminated. If not, if we cannot be practically certain that an explosion will not or cannot occur in the next case where ethylene is administered, I, at least, do not feel justified in authorizing the use of this anesthetic.

Possibly I am ultraconservative in my preference for methods of anesthesia. Perhaps some of this dislike of present day anesthesia is due to difficulties at once presented when one seeks the cause of the explosion. Like all of you, I have studied physics and chemistry, but I, at least, am far from being a physicist or chemist. And one would feel more comfortable about the whole problem if the manufacturers of the anesthetic machines, the physicists and chemists called in consultation would agree, but they do not. One claims that the cause of this and all similar accidents is the following. Another expert denies this and offers another explanation. I must confess that all this leaves me cold and with a feeling that I shall wait a while before resuming the use of this very inflammable anesthetic agent. However, I have given the problem of what caused the explosion considerable thought, and I give you my conclusions for what they are worth.

Undoubtedly anesthetic explosions of inflammable gas usually come from electrostatic sparks generated from without or within the machine. We all know what happens when we walk across the carpet in our homes in dry winter weather and bring a finger close to the radiator or electric light. The electric charge on our bodies jumps through the air in the form of a spark. This we know but we have had no necessity of applying such knowledge to the operating room where this static electricity may be accumulating. This is because up to a short time ago we were using either nitrous oxide and oxygen which is non-explosive or the drop method of etherization in which ether mixed with the oxygen of the air does not explode, even if conditions for static electricity be favorable.

This comparatively new anesthetic, ethylene, is highly inflammable and explosive when diluted with oxygen, and electrostatic charges are the common causes of the explosions. This has been recognized and provided against in modern hospitals. The methods adopted are well set forth in an article by Dr. Isabella C. Herb, chief anesthetist of the

Presbyterian Hospital, Chicago, published in the Journal of the American Medical Association, December 5, 1925. In brief, the operating room floor, the different parts of the gas machine, the operating table, and the patient are all grounded, so that electrostatic charges will be rendered harmless. Temporarily a sheet of steel was installed in the floor of the operating room, to be replaced by a floor of small squares of terrazo, separated by narrow brass strips.

One can readily see that the expense would prevent most established hospitals from installing such floors in their operating rooms. To put it another way, the hospital authorities probably would object to this extra expense in order to insure the safe use of a very explosive anesthetic mixture provided other safe anesthetics could be substituted. As an example I might cite the University of Michigan Hospital. Here there are eleven operating rooms in constant use on one floor. To install such floors referred to above in anesthetizing rooms, halls and operating rooms which practically have just been built would entail an expense which the authorities would hesitate to authorize unless no other anesthetic but ethylene could be used.

Yet that is not the whole story. As C. H. Wardell, Jr., has pointed out in his article entitled "Minimizing the Fire and Explosion Hazard of Anesthetic Agents," published in the March-April, 1928, issue of *Current Researches in Anesthesia and Analgesia*, such grounding devices referred to above are not enough. The operating rooms must be equipped with a humidification system whereby the operating rooms can be maintained at 60 per cent relative humidity, since the chances of electrostatic charges are greatly reduced in such an atmosphere. Yet it may not be amiss to state that when our accident occurred it was a rainy night, with probably a relatively high humidity within the delivery room. At least, the weather was not dry and cool when electrostatic sparks are most easily produced.

Yet even if we have adopted all these precautions to prevent electrostatic discharges, we have not finished. Professor Williams and his coworker on this problem, Dr. Franklin D. Johnston, point out that the greatest danger of static accumulation is on the inside of the rebreathing rubber bag, and they think that the movements of this bag, a rubber glove in the case of our explosion, were responsible for the accident. Professor Williams would substitute a manometric arrangement for the rubber glove while Dr. Johnston would prefer to try the effects of a radio-active substance to avoid static accumulation. Even with these precautions, the human equation cannot be eliminated. For example, undoubtedly after the terrible experience of the Cleveland Clinic disaster, it would be possible to guard against a similar accident, provided those carrying out orders were never heedless or careless. The heads of the clinic cannot go into the basement and see that fire doors are closed or that steam pipes do not leak. Neither can you nor

I find time or have the patience to examine operating room fixtures and anesthetic machines to guard against defective grounding. The probable result will be that a less dangerous x-ray film will be substituted for the one now in use and that for the large majority of hospitals, anesthesia will be accomplished with a less dangerous agent than ethylene.

It must not be forgotten that while nitrous oxide-oxygen mixtures are nonexplosive, the same is not true when ether is mixed with oxygen or when nitrous oxide-oxygen-ether mixtures are administered through any of the anesthetic machines.

The conscientious surgeon is not comforted by the fact that explosions are not likely to occur more frequently than so many times in so many hundreds or thousands of cases if the proper precautions are taken. Unless he is certain that an explosion will not occur in the next case where these explosive mixtures are employed, he will use another anesthetic free from the possibility of explosion if ordinary precautions are employed. This course I have been obliged to pursue since I abandoned ethylene. I must say that my present frame of mind toward general anesthesia is so free from anxiety, and the results are so satisfactory, that I shall have to be convinced that all dangers have been removed from the administration of explosive gases through anesthetic machines, before I shall change my present anesthetic technic which is as follows: The induction is made with nitrous oxide-oxygen mixture. This anesthetic is continued for short operations. For longer operations or for abdominal or pelvic work where relaxation is desired, the anesthetist turns to the open mask drop ether method, no ether mixture being allowed in the gas machine. Toward the close of other than short operations nitrous oxide-oxygen anesthesia may be resumed at the direction of the operator who notifies the anesthetist that from the operative standpoint ether is no longer needed. Here again no machine ether mixture is allowed.

In obstetric work, ether on the open mask is the anesthetic of choice. I have employed this method for obstetric analgesia and anesthesia for years with best of results. I have no objections to chloroform, but it is not quite as safe as ether, and experience should be gained in the use as far as possible of one anesthetic. In tropical climates for obvious reasons one must use chloroform in preference to ether.

May I also make a plea for the use of ether administered by the simpler methods on the ground that the student should be taught a simple effective method of general anesthesia, since only about 40 per cent of deliveries occur in hospitals. Only under exceptional circumstances can complicated gas machines be taken to private houses. Let us not do anything to make the practice of medicine any more complicated than it is only too rapidly becoming.

## SUMMARY AND CONCLUSIONS

1. Ethylene is an exceedingly inflammable and explosive gas when mixed with oxygen or ether.

2. Explosions may occur in the use of this anesthetic through electrostatic charges unless extraordinary precautions are taken to see that everything that has to do with anesthetic machine and surroundings is grounded.

3. Even then, there is a possibility of an explosion from within the gas machine as it is at present built.

4. It would seem best for the present at least to return to the use of nitrous oxide-oxygen gas and of ether given by the drop method, no ether mixture being allowed in the gas machines.

5. A return to simpler methods of anesthesia will enable the student to be instructed better in general anesthesia and make it possible for the surgeon to control anesthesia or at least to keep in close touch with the anesthetist during its administration.

6. The open mask administration of ether is best for analgesia and anesthesia in the second stage of labor.

7. In obstetrics complicated methods of anesthesia should not be taught to undergraduates or interns. The simple methods will be more useful for deliveries in private homes where about 60 per cent of deliveries still occur.

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DeGaris, Mary: Painless Labors—Their Occurrence, Their Interpretation and Their Adoption as a Standard, *Brit. M. J.* 2: 745, 1928.

A résumé of the literature and also fourteen histories of recent cases are presented. Some obstetricians deny the possibility of painless labors in a healthy woman. MacKenzie's theory that pain is a viscus-sensory reflex occurring during labor is well accepted.

Painless labors are classed as (1) pathologic labors, tabes, toxemias, etc.; (2) normal painless labors, healthy women, (a) type resembling defecation, (b) sleeping labor.

The symptoms are the same as in an average labor, even to fatigue which occurs not uncommonly. The doctor or nurse may pay little attention to the mother's sensations and she is not always certain of the impending condition.

The absence of pain is not sufficient to brand a labor as abnormal, it may be unusual but it is not necessarily pathologic. Since the uterus is like the other hollow viscera, and has the same physiology, why should all uterine contractions be painful? Why consider pain as a necessity to childbirth? Why not seek the cause of pain rather than that of its absence? It might be possible to bring the pains of labor under control by dealing with the cause instead of using palliative methods, such as anesthesia.

ADAIR-HESDORFER.

## PROLIFERATIVE OVARIAN TUMORS

A CLINICAL AND PATHOLOGIC STUDY OF 435 CASES TREATED BETWEEN  
1875 AND 1928 AT THE CLINIC OF THE FREE HOSPITAL FOR WOMEN

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**D**ERMOID cysts or ovarian teratomas, pseudomucinous cystadenomas, benign papillary serous cystadenomas, malignant papillary serous cystadenomas or ovarian carcinomas, fibromas, sarcomas and ovarian endometriomas are the usual proliferative tumors of the ovary. Between 1875 and 1928, 522 cases of proliferative ovarian tumor or tumors have been treated at this clinic, and of these, 85 have been private cases of Drs. William P. Graves and Frank A. Pemberton, treated between 1902 and 1928. Table I shows the distribution of the tumors.

TABLE I

DISTRIBUTION OF TUMORS	NUMBER OF CASES
Dermoid cysts alone (5 were bilateral)	97
Pseudomucinous cystadenoma of one ovary and bilateral dermoid cysts	2
Pseudomucinous cystadenoma of one ovary; dermoid cyst of the other	1
Benign papillary serous cystadenoma and dermoid cyst of same ovary	1
Pseudomucinous cystadenomas alone (8 were bilateral)	108
Pseudomucinous cystadenoma of one ovary; fibroma of other	3
Pseudomucinous cystadenoma and sarcoma of same ovary	1
Pseudomucinous cystadenoma of one ovary; sarcoma of the other	1
Benign papillary serous cystadenomas alone (21 were bilateral)	70
Benign papillary serous cystadenoma and fibroma of same ovary	1
Benign papillary serous cystadenoma of one ovary; fibroma of other	1
Benign papillary serous cystadenoma and fibroma—bilateral	1
Benign papillary serous cystadenoma of one ovary; endometrioma of other	1
Carcinomas alone (41 were bilateral)	84
Carcinoma of one ovary; endometrioma of other	3
Bilateral carcinoma; sarcoma of one ovary	1
Bilateral carcinoma; bilateral fibroma	1
Fibromas alone (4 were bilateral)	47
Bilateral fibromas; fibrosarcoma of one ovary	1
Sarcoma alone	10
Bilateral endometriomas	34
Unilateral endometriomas	53
Total number of cases	522
Total number of tumors	665

Since the ovarian endometriomas have been reviewed in a recent paper (AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY 17: 806, 1929), they will not be analyzed in this report. The very frequent finding of beginning papillary growth in their walls, however, and their more than occasional association with ovarian carcinomas should be emphasized as indicating a possible etiologic relationship.

In classifying these tumors no difficulty was encountered with the dermoids, fibromas or sarcomas. The cystadenomas, on the other hand, were very difficult to group and some cases, of necessity, were placed more or less arbitrarily. A definite decision as to whether some papillary cystadenomas were benign or malignant could not be made, even though the operative findings, the pathologic picture, and the results were carefully studied. Similarly, it was at times practically impossible to decide whether a cyst was of the pseudomucinous or serous type, for elements of both could be found. Furthermore, in a number of instances it could not be determined whether the malignant ovarian cyst was pseudomucinous or serous in origin or neither.

#### DERMOID CYSTS OF THE OVARY

Since the mesoderm and entoderm as well as the ectoderm are represented in these tumors, teratoma is the more correct term. Dermoid, however, is more usual. This report covers 101 cases.

*Family History:* tuberculosis, 6.9 per cent; malignant disease, 6.9 per cent.

*Past History:* 26 patients had had previous operations, of which 17 had been pelvic. Two had had an ovarian tumor removed.

*Age on Admission:* youngest, fourteen; oldest, sixty-five; 63.3 per cent were between the ages of twenty-four and forty inclusive.

*Marital Condition:* unmarried, 22.7 per cent; sterile, 16.1 per cent. The average number of pregnancies per married patient was 3.7; of children, 3.1.

#### *Menstruation:*

Before puberty	1	Essential dysmenorrhea	5
Past the menopause	11	Acquired dysmenorrhea	28
Menopause before forty-five	5	Menorrhagia	14
Dysmenorrhea worse on same side as tumor	6	Metrorrhagia	13

#### *Complaints:*

Backache	24	Flowing	6
Pain in right side	22	Flowing after menopause	2
Pain in left side	22	Sterility	3
Pain in lower abdomen	20	"Falling of womb"	10
Swelling of abdomen	11	Attacks of right-sided pain	4

One patient, whose seven-centimeter cyst had a twisted pedicle, had had pain in the left side increasing in severity for six days. In 40 per cent of cases the symptoms were directly referable to the quadrant in which the dermoid was found, despite the fact that some of the tumors seemed too small to make their presence known.

The duration of symptoms varied from a few weeks to over ten years. In the majority of cases the duration was less than three years.

## OPERATIONS AND RESULTS

*Ovarian resections* were performed on 5 patients. Three are untraceable. One patient was four months' pregnant and well two years later; another was well twenty years later.

*Unilateral oophorectomy* was performed on 52 patients. Fourteen are untraceable. Operative deaths, 2 (circulatory collapse, patient aged 60; pneumonia, patient aged thirty). Four patients died from seven months to twenty-nine years after operation—pneumonia, criminal abortion, influenza, and nephritis. Thirty-two patients were well from six months to twenty-five years later. Five had had 12 normal pregnancies and deliveries. A sixth patient, who had had a tubal pregnancy on the same side as the dermoid, had a second tubal pregnancy excised six years later and was well fourteen years later. Four other patients had later operations—cholecystectomy, 2; radium for flowing, 1, and excision of cyst of remaining ovary, 1.

*Supravaginal hysterectomy and bilateral oophorectomy* were performed on 39 patients. Eight are untraceable. Five patients died from three months to nine years later—metastatic carcinoma of endometrium, pneumonia, nephritis, carcinoma of the colon, and appendicitis. Twenty-six were well from one to fifteen years later. Two of these complained of excessive obesity.

*Complete hysterectomy* was performed on 2 patients. (Carcinoma of endometrium and dermoid.) One is untraceable. The other is well six years later.

*Vaginal section and drainage* (1878) were performed on 1 patient. The patient died of carcinoma of the breast thirteen years later.

*Drainage through rectum for dermoidrectal fistula* (1882) was performed on 1 patient. The patient was improved six months later.

*Two-stage unilateral oophorectomy* was performed on 1 patient. Patient died of shock following second operation. The tumor was dumb-bell-shaped, 24 centimeters in greatest diameter, one locule being in the pelvis, the other extending through the greater sciatic foramen and distending the buttock.

## PATHOLOGY

The tumors revealed nothing unusual. Entodermal derivatives were only rarely found. There was no ovarian malignancy. In 28 cases the dermoid was an incidental finding, the operation being performed for prolapse, fibroids, pelvic inflammation, carcinoma of the endometrium, flowing, and tubal pregnancy. In these cases the tumors were small and usually gave no symptoms directly referable to the ovary. On the other hand, there were a few cases in which the dermoid, though small and nonadherent, seemed to cause one-sided pain.

The tumors were bilateral 8 times. In 2 of these one was a part of a large pseudomucinous cyst and in a third one was part of a fifty-pound simple serous cyst. In 2 cases the dermoids were a part of large benign papillary cysts. The size of the dermoids varied from 1 to 35 centimeters; 83 per cent were between 3 and 12 centimeters in greatest diameter.

In 32 instances there were adhesions between the tumor and surrounding structures. These were usually not dense. The cyst was ruptured at operation 3 times, with no ill consequences from spilled contents. Fibroids were found in 15 patients (14.8 per cent), and gallstones were found in 4.

#### SUMMARY AND CONCLUSIONS

1. Abnormality of menstruation was present in 51.6 per cent of patients.
2. Eight patients had benign ovarian cysts in addition to the dermoids.
3. The operative mortality was 2.9 per cent.
4. The results of operation, in the absence of other pathology, were uniformly good since only 2 patients had later pelvic operations.
5. In 7 patients there occurred after operation 15 pregnancies of which 12 resulted in normal labors.
6. Malignant ovarian disease in this series was conspicuous by its absence.
7. In the absence of other pathologic conditions the treatment of ovarian dermoids should be operative and as conservative as possible.

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#### PSEUDOMUCINOUS CYSTADENOMA

There were 116 cases with this type of tumor. In 23 instances, before 1902, the diagnosis was not confirmed microscopically, so there is probably a small percentage of error in the following figures.

*Family History:* tuberculosis, 6 per cent; malignant disease, 4.3 per cent.

*Past History:* 6 patients were tapped one or more times before operation.

*Age at Operation:* youngest, eighteen; oldest, seventy-three. Forty-three, 34.7 per cent, were between forty-five and fifty-five years old.

*Marital Condition:* unmarried, 24.3 per cent; sterile, 16 per cent. The average number of pregnancies was 3.3, of children, 2.7.

##### *Menstruation:*

Past the menopause	37	Irregular menstruation	23
Menopause before forty	4	Dysmenorrhea	11
Menopause before forty-five	16	Menorrhagia	2
Flowing after menopause	10		

##### *Complaints:*

Swelling of abdomen	81	"Falling of womb"	5
Pain in lower abdomen	58	Pressure in pelvis	5
Backache	19	Flowing	5

In 84 cases the duration of symptoms was less than three years.



## OPERATIONS AND RESULTS

*Resections of ovary* were performed on 2 patients. One was untraceable. One was well four years, five months later.

*Unilateral oophorectomy* was performed on 47 patients. Operative deaths, 4 (2 of surgical shock and 2 of peritonitis, all before 1900). Fourteen were untraceable. Six patients died from eight months to thirty-one years later—recurrent malignant pseudomucinous tumor, pneumonia, "dysentery," "arteriosclerosis," cerebral hemorrhage, and "old age." Twenty-three patients were well from six months to thirty years later. Four had had eight pregnancies, seven of which resulted normally. One had a hysterectomy for fibroids twelve years after operation and was well four years later.

*Supravaginal hysterectomy and bilateral oophorectomy* were performed on 64 patients. There was 1 operative death in 1881—surgical shock. Twelve were untraceable. Nine patients died three months to twenty-six years later, recurrent carcinoma of the endometrium, recurrent malignant pseudomucinous tumor (4 cases), nephritis, "arteriosclerosis," "colitis," and cerebral hemorrhage. Two are living with recurrence less than one year after operation. Forty patients were well from six months to fifteen years later, 1 having had an operation for "carcinoma of the rectum" five and a half years later.

*Complete hysterectomy* was performed on 3 patients. One died of recurrence of the ovarian tumor one year, four months later. The second patient, with carcinoma of the cervix also, had a recurrence but was living one year, three months after operation. The third, with carcinoma of the endometrium, was well six months later.

## PATHOLOGY

The typical pseudomucinous cystadenoma is a large, ovoid, white, yellowish white, pale or gray blue tumor with a smooth surface which is bumpy due to the contained locules. Though the tumor does occasionally consist of one locule (12 of this series were unilocular) or a few locules, it is most often made up of at least 20 or more which vary in diameter from microscopic dimensions up to 20 centimeters or more. The contents are characteristically colorless, translucent, and slimy. They may, however, be of a watery consistency (6 of this series contained serous fluid) or may form a firm gelatinous coagulum. Instead of colorless they may be opalescent, dirty yellow, olive green, brownish red, or some intermediate shade.

Microscopically the typical picture is of a fibrous cyst wall on the inner surface of which is a single layer of tall columnar cells with clear cytoplasm and basal nuclei. Sometimes the cells contain a globule of pseudomucin. Occasionally there are tufts made up of cells or fibrous papillae covered with them. (Twenty-eight cysts of this series were

papillary.) At times there may be seen in the same section, especially when papillae are present, cuboidal cells with central nuclei and pink cytoplasm. These are characteristic of the serous cystadenomas and make a definite diagnosis difficult. When these cysts are malignant, the cells most often do not show their pseudomucinous character, the diagnosis being made by the finding of characteristic epithelium in another portion of the tumor.

These cysts are usually larger and contain more locules than the serous type; in this series the smallest was 2 centimeters in greatest diameter, the largest, 55. Seventy-seven, 62 per cent, were between 15 and 35 centimeters. It is common for their pedicles to be long and well developed. More or less twisting is usual, but in this series no acute symptoms from twisted pedicle occurred. More or less necrosis, however, was not uncommon. Adhesions, usually not dense or extensive, were found in 51.7 per cent of cases.

Fifteen cases of pseudomucinous cystadenoma, 12.9 per cent, had definitely malignant tumors. There were 4 other cases the gross findings and clinical course of which indicated a benign growth, although microscopically it was impossible to demonstrate that the tumors were definitely benign. They were of very low malignancy. Three of the 15 patients with frankly malignant tumors had bilateral tumors, but the disease was so far advanced that it seemed probable that one ovary was involved secondarily. Five more had metastasis at the time of operation. These all died of recurrence. Two others are untraceable. The remaining 5 were well from one to sixteen years after operation. In all these there was no metastasis found at operation and in all but 1 the tumors had been removed intact without rupture. In this 1 patient, well sixteen years later, the tumor had been ruptured and it appeared malignant under the microscope. Either there had been no viable cells in the spilled contents or the patient exhibited a spontaneous resistance. At a supravaginal hysterectomy for fibroids eleven years later there was no evidence of any recurrence.

Pseudomyxoma peritonei found in 2 of the malignant cases demonstrated a diffuse myxomatous peritoneal implantation. Three benign cases showed this condition. There were 2 operative deaths (before 1900); the other is apparently well one year, six months after operation.

Ascites occurred in 5 malignant and in 6 benign cases.

*Rupture at operation:* In 19 benign cases the tumors were found ruptured on opening the abdomen or when the trocar was used at operation, or were ruptured unintentionally due to the presence of necrosis and adhesions. Follow-ups from six months to thirty-one years indicated no later ill effects. With the exception of the 1 case mentioned above, metastasis was already present at the time of rupture in those with malignant cysts.

## ASSOCIATED PATHOLOGY

Fibroids	23	Diffuse uterine endometrioma	4
Endometrial polyp	8	Fibroma of opposite ovary	3
Procidencia	6	Bilateral dermoid cysts also	2
Cervical polyp	4	Carcinoma of endometrium	2
Nineteen-pound simple serous cyst of other ovary			1
Sarcoma of same ovary			1
Sarcoma of other ovary			1
Dermoid of other ovary and carcinoma of endometrium			1
Carcinoma of the cervix			1

## SUMMARY AND CONCLUSIONS

1. The opposite ovary was normal in 87 per cent of cases. In 3 other cases malignant involvement of the other ovary was probably secondary.

2. There were 5 operative deaths, all before 1900 (4.3 per cent).

3. Malignant pseudomucinous cystadenoma was diagnosed in 12.9 per cent of this group.

4. There is evidence that some of the malignant tumors were originally benign.

5. At the time of operation 20 patients of this series, 17.2 per cent, had malignant disease in the pelvis—cervix, endometrium, and ovary. Another patient had carcinoma of the rectum at a later date.

6. In the absence of other pathology conservative operation gave just as good results as radical, i.e., the patients were cured symptomatically and no further ovarian trouble developed. Furthermore, 4 of these patients had eight pregnancies, seven of which were normal.

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## BENIGN PAPILLARY SEROUS CYSTADENOMA

These tumors are characterized grossly by a thin, pale blue wall which is often necrotic and adherent to surrounding structures, by being generally smaller than the pseudomucinous cysts and by their proclivity to burrow between the leaves of the broad ligament. They are frequently bilateral—in 29.4 per cent of this series of the time of operation. Their contents are most often serous or watery and of a color varying from pale yellow to brown or red depending on the amount and kind of blood pigment. Their lining may be nearly all smooth with the exception of a few localized or scattered, pale white papillae less than 1 centimeter in diameter, or it may be covered with many small granular or large fungating excrescences which grossly make malignancy seem probable. In some cases the cyst is filled with a fungating, necrotic, friable mass. Microscopically the fibrous cyst wall, often showing hyaline degeneration, extends into the cyst in the form of tough papillae of varying sizes and shapes. These are covered with a single layer of cuboidal cells with central nuclei and pink-staining cytoplasm. These cells may be heaped

up in places, especially at the bases or tips of papillae. They may also show ciliation which is regarded as a sign of potential malignancy. It is sometimes difficult to determine whether a given tumor is definitely benign or of low malignancy, especially as the microscopic picture may vary in the same tumor. This report deals with 74 cases of this type of tumor. In every instance the diagnosis was confirmed microscopically.

*Family History:* tuberculosis, 6 per cent; malignant disease, 8 per cent.

*Past History:* oophorectomy for cyst, 2 cases; hysterectomy without removal of ovaries, 1 case.

*Age on Admission:* youngest, seventeen; oldest, sixty-nine. There was no marked incidence at any age in this group.

*Marital Condition:* 15 per cent were single; 17.7 per cent were sterile. The average number of pregnancies was 2.3, of children, 1.7.

*Menstruation:* 30.1 per cent of patients had passed the menopause. Dysmenorrhea was complained of by 29.4 per cent, irregular or profuse menstruation by 39.4 per cent.

*Complaints:*

Swelling of abdomen	25	Pain in right side	7
Pain in lower abdomen	17	"Falling of womb"	9
Backache	14	Flowing after menopause	5
Pain in left side	9		

The duration of symptoms was less than three years in 65 per cent of cases.

#### OPERATIONS AND RESULTS

*Exploratory laparotomy and biopsy* were performed on 1 patient.

This patient had abdominal swelling and marked uterine prolapse. On opening the abdomen free fluid was encountered and the peritoneum was covered with papillary excrecences. There were bilateral ovarian masses in the pelvis, which were densely adherent. Grossly it was the picture of advanced ovarian malignancy. A specimen was taken for biopsy and the incision closed. The specimen was found to consist of fibrous tissue covered with a few inactive, low cuboidal cells. The patient is alive and working twelve years, three months later. If the biopsy had not shown the growth to be benign, this case would have passed as an example of spontaneous cure. I have been unable to find a single case of advanced ovarian, or any other malignancy that has undergone spontaneous cure when the microscopic picture was undoubtedly malignant.

Twelve years, eight months after operation this patient was brought to the hospital in extremis and died of intestinal obstruction. She had refused treatment. Postmortem abdominal exploration revealed widespread adhesions. The uterus was completely atrophied; the ovaries could not be identified. There was no gross or microscopic evidence of the previous tumor.

*Ovarian resections* were performed on 7 patients. One is untraceable. The others were well four months to ten years later. There was 1 normal pregnancy.

*Unilateral oophorectomy* was performed on 19 patients. Four are untraceable. One patient died one year later after a third operation for

severe pelvic inflammation. Fourteen were well from ten months to nineteen years later. There was one successful pregnancy.

*Supravaginal hysterectomy and bilateral oophorectomy* were performed on 43 patients. There were 2 postoperative deaths from peritonitis. Six are untraceable. Five died one and one-half to seventeen years later—cerebral hemorrhage, "heart disease" (2 cases), pneumonia, and "arteriosclerosis." One of these had been operated on successfully for intestinal obstruction four years, four months after hysterectomy. Thirty patients were well from five months to twenty-three years after operation, 1 patient having had a breast amputated for carcinoma six years after operation.

*Complete hysterectomy* was performed on 4 patients. One died of carcinoma of the cervix eight months later. The others, who had had carcinoma of the endometrium, were well eight months, six years and fourteen years later.

#### PATHOLOGY

There were adhesions of the tumor to surrounding structures in 61.6 per cent of cases. They resulted in rupture of the cyst in 5 cases. Follow-ups for from seven to nineteen years indicate that spilling of benign cyst contents has no ill effect.

In 7 cases the cyst contents were of the pseudomucinous type. It is of interest that the epithelium of 3 of these tumors showed an activity that approached a low grade of malignancy more than in the cysts with serous contents—except for 2 whose epithelium was ciliated.

A twisted pedicle was found at operation 4 times. There had been no acute symptoms demanding immediate operation.

Eight of the cysts were monolocular; the remainder consisted of at least two locules. As contrasted with the pseudomucinous cysts, however, the serous cysts were "pauci-locular." They varied in size from 2 millimeters to 30 centimeters in greatest diameter, 24.7 per cent being over 15 centimeters.

In 2 cases there were papillary excrescences on the outer surface of the tumor; in 2 others there were implants on the peritoneum. These patients were well three months to fifteen years later,

Ascites was found three times. It did not effect the prognosis as to cure.

#### ASSOCIATED PATHOLOGY

Fibroids	26	Fibroma of opposite ovary	1
Endometrial polyp	4	Bilateral fibroma of ovary	1
Cervical polyp	3	Fibroma of same ovary	1
Discrete uterine endometrioma	2	Dermoid of same ovary	1
Diffuse uterine endometrioma	1	Carcinoma of the cervix	1
Endometrioma of opposite ovary	1	Carcinoma of endometrium	3

## SUMMARY AND CONCLUSIONS

1. Menstrual abnormality was complained of by 68.8 per cent of patients.

2. Bilateral tumors developed in 30.6 per cent of cases.

3. In 25 instances the finding of a benign papillary cyst was accidental, the operations being performed for prolapse, fibroids, carcinoma, pelvic inflammation, dysmenorrhea or sterility.

4. The operative mortality was 2.7 per cent.

5. Thus far the results of conservative operation have been as satisfactory as those of radical operation. Two normal pregnancies occurred. However, the tendency of these tumors to become bilateral should be remembered when conservative operation is contemplated.

6. Spilling of the cyst contents in 4 cases had no early or late ill effect.

7. Malignant disease was present at operation, or developed later, in 6.8 per cent of cases.

8. Although these tumors are morphologically related to and sometimes the forerunners of the malignant serous cysts, as yet no patient of this group, treated conservatively, has been known to develop a malignant cyst.

\* \* \* \*

## MALIGNANT PAPILLARY SEROUS CYSTADENOMAS

As already indicated these cysts have features in common with both the malignant pseudomucinous and the benign serous cysts. This is not remarkable since in the ovary all epithelial elements and their derivatives have the same ancestry. This group includes 87 cases of malignant papillary serous cystadenoma, 1 of intracystic solid carcinoma, and 1 solid carcinoma. In all but 3 cases the diagnosis was made or confirmed by microscopic examination.

*Family History:* tuberculosis, 6.8 per cent; malignant disease, 6.8 per cent.

*Past History:* 1 patient had had a hysterectomy without removal of ovaries at the age of forty-one; 4 patients had been tapped.

*Age on Admission:* youngest, twenty-two; oldest, eighty-six. Over half were between the ages of forty and fifty-five.

*Marital Condition:* 23.5 per cent were single; 23.5 per cent were sterile. The average number of pregnancies was 3.8, of children, 2.

*Menstruation:* 33.7 per cent had passed the menopause, this occurring in 4 cases at the ages of thirty-four, forty-two, forty-four and forty-five respectively. Of the remainder 45.7 per cent had some menstrual abnormality.

*Complaints:*

Swelling of abdomen	57	Flowing	7
Pain in lower abdomen	40	Pain in right side	6
Flowing after menopause	7	Pain in left side	5

The duration of the complaint was less than one year in 47 per cent of cases, less than two years in 66 per cent.

#### OPERATIONS AND RESULTS

One patient died two weeks after admission. Autopsy revealed the ovarian disease.

*Exploratory laparotomy only*, the disease being found too advanced for further procedure was done on 10 patients. There were 2 operative deaths, of surgical shock (1886 and 1896). Two are untraceable. Five died of recurrence one month to five years, five months later. One patient with advanced disease but no ascites was alive three years after operation.

*Unilateral oophorectomy* was performed on 16 patients. Operative death, 1—surgical shock. One is untraceable. Nine died of recurrence less than four years later. One of these had had a cyst of the other ovary removed. One patient died of "angina pectoris" four years, five months after operation. There were 2 with recurrences living a year and a half later. Another with a recurrence was alive six years, four months after operation, having had tumor of the other ovary removed. One patient was well three years later.

*Bilateral oophorectomy* was performed on 9 patients. There were 3 operative deaths, before 1897, due to sepsis and peritonitis. The others died of recurrence less than two and a half years later.

*Supravaginal hysterectomy and bilateral oophorectomy* were performed on 49 patients. Four died of surgical shock. Four are untraceable. Seventeen died of recurrence less than three and one-half years later. Five with recurrence are living one to three years later. Nineteen patients were well from six months to thirteen years after operation—10 of these had passed the five-year interval.

*Complete hysterectomy* was performed on 4 patients. Three are untraceable. The other died of recurrence seven years, seven months after operation.

#### PATHOLOGY

It is necessary to emphasize again the difficulties of classification and of arriving at a conclusion as to whether or not a borderline case is malignant. In one instance some definite pseudomucinous cells were found in the same tumor along with the typical picture of benign papillary serous cyst and with papillary adenocarcinoma. In 7 cases the cyst contents were pseudomucinous, not serous, but the microscopic picture was characteristic of the serous cystadenomas. Three of these were graded as borderline or very low malignancy; the patients were well four to ten years after operation. In all cases the grade of malignancy, based on the microscopic appearance, varied greatly not only in

different tumors but even in the same tumor. This was demonstrated to some extent clinically, for the length of life of patients with equally poor prognoses at the time of operation varied markedly. In some instances the picture of typical benign, papillary cystadenoma was found beside that of papillary adenocarcinoma; in other instances, usually more advanced cases, no stages suggesting transition from a benign to a malignant condition could be found. The 2 patients with solid carcinoma microscopically were well five and eleven years respectively after operation. At operation they both had ascites but no evidence of metastasis, and the tumors were removed intact.

The greatest diameter of the smallest cyst was 3 centimeters, of the largest, 50. Thirty-six per cent were over 15 centimeters in greatest diameter. Although they were mono- (7), bi- (3) and multilocular (79), none consisted of over 15 to 20 locules. Like the benign, papillary cysts they were paucilocular as compared with the pseudomucinous cysts. The serous contents varied from clear and transparent to opalescent and cloudy and their color was of all shades from pale yellow to green, brown, and red. Varying amounts of friable, dirty white, papillary fungus growths were contained.

Adhesions of the tumor or tumors were present in 89.7 per cent of cases. These were most often extensive and dense making the removal of an intact cyst extremely difficult. Furthermore the cyst walls were often necrotic, a condition which probably antedated the adhesions.

The tumors were bilateral in 43 cases, or 48.3 per cent. These were found often enough in cases without extension or metastasis to indicate that the growth was primary in each ovary, unless the possibility of blood or lymph metastasis be considered.

#### ASSOCIATED PATHOLOGY

Fibroids	25	Carcinoma of endometrium	2
Endometrial polyp	5	Double uterus	1
Endometrial polyp of other ovary	3	Complete vaginal atresia	1
Diffuse uterine endometrioma	2	Sarcoma of same ovary	1
Endometrioma of posterior wall of uterus			1
Bilateral ovarian fibroma			1

In the 2 cases of both ovarian and endometrial carcinoma neither carcinoma was secondary to the other so far as could be determined.

At the time of operation the prognosis was poor in 68 of the 89 cases of this series, due to the advanced stage of the disease, to metastasis, to the finding of a cyst already ruptured or to the rupture of a cyst at operation. Ascites was present in 30 cases. Three patients of this group of 68 were alive and well four to ten years later. Their tumors were definitely of very low malignancy.



The prognosis in the remaining 21 cases was not frankly poor. Six had ascites. The contents of none of the cysts were spilled in the peritoneum. Only one is known to have died of recurrence. Eleven were well three to fourteen years later.

#### SUMMARY AND CONCLUSIONS

1. The percentage of sterility was 23.5; 23.5 per cent were single; 45.7 per cent had abnormal menstruation and 33.7 per cent had passed the menopause. This type of ovarian disease seems to be associated with lack of function, abnormal function, and with involution.

2. There is evidence that not all of these tumors are malignant from their inception.

3. Those patients who had bilateral tumors at operation or who developed a second one later comprise 50.5 per cent of the series.

4. The microscopic degree of malignancy was of some value in prognosis.

5. Taking the series as a whole, of those traceable, at the end of three years 33 per cent were alive and of those traceable at the end of five years 19.6 per cent were alive. Less than 10 of the series, i.e., about 10 per cent, may safely be considered cured.

6. Ascites was present in 40 per cent of patients, 3 of whom are now considered cured. Ascites in itself does not affect the prognosis.

7. There were 10 operative deaths, 11.3 per cent, five of which occurred before 1897.

8. Every effort should be made to avoid spilling cyst contents in the peritoneal cavity. If the tumor happens to be microscopically malignant, previous abdominal paracentesis or rupture at operation eliminates all chance of cure.

9. Since this type of tumor is so often bilateral, since the patients are sterile or beyond the childbearing age and since there is usually considerable associated pathology, the conservative procedure is hysterectomy. The diagnosis, gross and microscopic, should be made at the time of operation.

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#### OVARIAN FIBROMAS

Fibromas were found in 55 cases. It was incidental in 34 instances, operation being performed primarily for fibroids, prolapse, dysmenorrhea, sterility, retroversion, large ovarian cyst, carcinoma or appendicitis—and in these cases the tumors were too small (less than 6 centimeters) to cause the symptoms complained of.

*Family History:* tuberculosis in 3.6 per cent; malignant disease in 7.2 per cent.

*Past History:* one patient had had unilateral oophorectomy; one had had hysterectomy without removal of the ovaries.

*Age at Operation:* youngest, 20; oldest, 78. In 58 per cent the tumors occurred between the ages of thirty and fifty.

*Marital Condition:* 20 per cent were single; 12.6 per cent were sterile. The average number of pregnancies was 3.2, of children, 2.6.

*Menstruation:* 27.2 per cent had passed the menopause; between 40 and 50 per cent of the others had some abnormality.

*Complaints:*

Swelling of abdomen	11	"Falling of womb"	17
Backache	12	Sterility	3
Pain in lower abdomen	21	Flowing	5

In 60 per cent of cases the duration of symptoms was less than three years.

#### OPERATIONS AND RESULTS

*Ovarian resections* were performed on 13 patients. One is untraceable. Eleven were well one to twelve years later. Two had had two normal pregnancies and three abortions. One died of carcinoma of the pancreas twelve years later.

*Unilateral oophorectomy* was performed on 12 patients. There was one operative death. Four are untraceable. One patient died of intestinal obstruction five weeks later; one, of pernicious anemia three and a half years later; one, of pulmonary tuberculosis sixteen years later. Four were well one to eleven years after operation.

*Supravaginal hysterectomy and bilateral oophorectomy* were performed on 28 patients. There was 1 operative death from pulmonary embolus. Six are untraceable. One died of pneumonia seventeen years later; the other is well six years later.

#### PATHOLOGY

Grossly the tumors were of a yellowish white color, firm and irregular. Their surfaces were smooth and glistening or rough and papillary. More or less cystic degeneration was found in the larger fibromas; hyaline degeneration was common. The smallest fibroma was 3 millimeters in diameter; the largest, 25 centimeters. Fifty-six per cent of the tumors were 5 centimeters or less in diameter. They were bilateral in 7 cases, or 12.7 per cent. Microscopically they consisted of connective tissue which showed a wide range of density and cell content. In 16 cases there were adhesions involving the tumor. Three patients had ascites.

#### ASSOCIATED PATHOLOGY

Fibroids	18	Carcinoma of endometrium	1
Endometrial polyp or polyps (14.5 per cent)	8	Benign papillary cyst, other ovary	1
Gland hypertrophy of endometrium	5	Benign papillary cyst, same ovary	1
Pseudomucinous cyst of other ovary	3		
Bilateral papillary serous cysts and bilateral fibromas			1
Malignant papillary cyst and bilateral fibromas			1
Fibrosarcoma of one ovary and bilateral fibromas			1

## SUMMARY AND CONCLUSIONS

1. Although none of the patients in this group who were submitted to conservative operation are known to have had further ovarian trouble, the frequency of menstrual abnormality and the associated pathology, both ovarian and uterine, indicate that the finding of a fibroma may be a danger signal pointing to possible serious disturbance.
2. The operative mortality was 3.6 per cent.
3. If there be no malignancy and no serious associated pathology, conservative operation is indicated for this type of tumor.

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## OVARIAN SARCOMAS

Sarcoma was diagnosed in 14 cases. The family and past histories were negative. Half of the patients were over sixty years of age. Ten, 3 of whom complained of flowing, had passed the menopause. Of the remaining 4, 1, nineteen years old, had acquired dysmenorrhea; the second, thirty years old, had not menstruated for sixteen months; the third, thirty-nine years old, had not menstruated for a year; the fourth, aged forty-five, had menstruated irregularly for one year. In 12 cases the duration of symptoms, abdominal swelling and pain, was one year or less.

## OPERATIONS AND RESULTS

In 1 case an advanced stage of the disease was found at exploratory laparotomy. The patient is untraceable.

*Unilateral oophorectomy* was performed on 4 patients. There was one operative death—from peritonitis. Two patients died of recurrence within one year; 1 was well six years later.

*Supravaginal hysterectomy and bilateral oophorectomy* were performed on 9 patients. Three died of recurrence less than one year later and 6 were well eight months to six years after operation.

## PATHOLOGY

Just as leiomyosarcomas are most often found in fibroids that show cystic or hyaline degeneration or calcification, so the ovarian sarcomas are often associated with fibromas having these changes. In the present group of which two were round-celled and 12 spindle-celled or fibrosarcomas, 9 showed hyaline degeneration, 3 cystic degeneration and 2 calcification. In some of the fibrosarcomas were found areas similar to the round-celled type.

Grossly some of the tumors resembled fibromas; others were friable and spongy. The smallest sarcoma was 1 centimeter in greatest diameter, the largest, 25. Adhesions of the tumor to surrounding structures were present in 11 cases. Ascites was present in 7.

## ASSOCIATED PATHOLOGY

Endometrial polyp or polyps	5 (35.6 per cent)
Multiple fibroids	3
Gland hypertrophy of the endometrium	1
Bilateral fibromas and sarcomas	1
Bilateral malignant papillary serous cysts	1
Pseudomucinous cystadenoma of same ovary	1
Pseudomucinous cystadenoma of other ovary	1

## COMMENT

In 2 instances the sarcomas apparently had a profound prohibitive effect on menstruation. An endometrial polyp was present in 5 of the 8 cases in which uterine cavities were examined.

## SUMMARY AND CONCLUSIONS

1. This paper consists of a clinical and pathologic analysis of the usual proliferative ovarian tumors treated at the Free Hospital for Women in a period of over fifty-two years.

2. With the exception of the dermoids the origin of the proliferative ovarian tumors seems to be associated with lack of ovarian function, abnormal ovarian function, and ovarian involution. The prolonged irritative effect of the contents of some benign cysts may be the stimulus to malignant change in certain instances. In other cases pressure or torsion results in a curtailed blood supply to an ovary or to a benign ovarian tumor. This is followed by hyalinization and calcification or necrosis. To survive, cells change their methods of metabolism and growth and a malignant tumor results.

3. No undiagnosed abdominal tumor should ever be tapped, for if it is malignant, tapping will reduce the possibility of cure to almost nothing.

4. Every effort should be made to remove ovarian tumors intact without spilling any of their contents in the peritoneal cavity. Immediately upon removal the tumor should be examined grossly and microscopically. If it is a dermoid, benign pseudomucinous cystadenoma or a fibroma, unilateral or bilateral, and there is no other pathologic condition, conservative operation is indicated. If it is a benign papillary serous cystadenoma and the other ovary appears normal, conservative operation, in the absence of other pathologic conditions, will depend on the patient's age and desire for pregnancy. If the other ovary is left, the patient should be watched for years. If the tumor is malignant, radical operation should not be deferred, even with a normal appearing opposite ovary. In every case the vagina, cervix, and uterine cavity should be routinely examined to rule out possible associated pathology.

5. Spontaneous regression of microscopically malignant ovarian tumor did not occur in any case of this series.

6. Postoperative irradiation in three malignant cases did not apparently affect the outcome.

7. The microscopic grade of malignancy is of some value in prognosis in a few cases.

I am grateful to Drs. William P. Graves and Frank A. Pemberton for the use of their private records and for their generous assistance.

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## THE ETIOLOGY OF ADENOMYOSITIS AND UTERINE FIBROMYOMA: AN HYPOTHESIS

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IN ANOTHER article I discussed the histogenesis of adenomyotic growths, and I now wish to touch upon the subject of their etiology. The latter is still more disputable than the histogenesis, and I would not have the temerity to tread upon this uncertain ground at all had not Sampson a short time ago advanced an etiology not only for endometriosis but for uterine fibromyomata as well.

Based upon his experiments published in 1918, showing that fluids forced into the uterine cavity may enter the venous sinuses of the wall, Sampson has stated that leiomyoma of the uterus may be due to local hyperplasia of the muscle cells in reaction to the stimulus of menstrual blood, which by a retrograde current has reached these particular areas. As proof of such an etiology in uterine fibromyomas, Sampson offers the observation that smooth muscle tissue in contact with heterotopic endometrial tissue often shows a tendency to grow. He believes that the cervix and tubes seldom produce fibromyomas because they do not menstruate, and that uterine fibromyomas are so much more common in the human female than in any other mammal because none of the latter menstruate. Aside from the fact that, as mentioned in the previous paper, there are justified doubts regarding the growth-producing properties of the menstrual blood, and the additional point that the apes menstruate, but rarely have uterine fibromyomata, there are other grave objections to this "menstrual blood" theory of Sampson. At the same time there can be no doubt either theoretically or logically that the etiology of endometrial growth wherever situated and uterine fibromyomas, must be closely connected, since these structures are all definitely müllerian tissue.

To arrive at a rational etiology of any condition, one must start with and carefully weigh those facts which are really known. In the case of adenomyositis, these are soon stated:

1. Adenomyositis occurs only in the female. (The case of adenomyositis in the urachus of a man fifty-five years old, reported by Kosłowsky, I regard not as an adenomyositis, but simply as an allontoic rest.)

2. Adenomyositis occurs only during the sexual life of the woman.

3. Adenomyositis regresses after castration or atrophy of the ovaries. There appear in the literature certain case reports (see Graves) which seem to contradict this last statement. Katz and Szenes, for instance, report that they were able to grow endometrium in both normal and castrated animals. Probably this can be explained, just as the continuance of menorrhagia following bilateral castration, as being due to the aberrant remnants of ovarian tissue. Persistence of chocolate cysts following x-ray and radium castration with atrophy of the uterine endometrium and uterine fibromyomata is also recorded. This is no proof against the truth of our third conclusion, since there is no evidence to show that these chocolate cysts are really still active. Such cysts filled with old blood would naturally take a long time to disappear; furthermore after x-ray or radium treatments, continued amenorrhea with a subsequent pregnancy is not unknown.

From the facts presented one truth stands out, namely that in some way or other the ovary is responsible for adenomyositis. Can we then find a concept which will offer a reasonable etiology for these growths? I believe I can venture an hypothesis which will at least theoretically explain not only the occurrence of adenomyositic lesions, but also their vagaries and perhaps also be applicable to the uterine fibromyomas.

Before taking up adenomyositis, let us review the reaction of the endometrium itself to ovarian influence. Before puberty there is no real endometrium, and after the action of the ovaries is lost, the endometrium atrophies. It can now be definitely stated that the monthly proliferative changes in the endometrium are based on follicular activity, and that the secretory or premenstrual changes are due to corpus luteum activity. That the substance producing, for instance, the decidual reaction in the premenstrual endometrium is carried by the blood stream was shown even before Allen and Doisy, before Frank and his collaborators and others demonstrated a female sex hormone in the blood, by the fact that it is around the small blood vessels in the form of a thinner or thicker mantle that the stroma cells of the uterine mucosa first acquire their decidual characteristics. This is an important point.

If, then, the ovarian hormone carried by the blood stream causes the endometrial changes, it is justifiable to assume, and this is supported by clinical and pathologic evidence, that the amount of hormone will, other things being equal, determine the amount of reaction shown by the endometrium. Increased follicular activity would lead to increased growth of the endometrium. Thus in the hyperplasia of the endometrium I have seen follicular cysts of the ovary associated in most cases. In fact, from the histologic picture alone of a slide showing a definite hyperplasia of the endometrium, I have felt so certain

that the ovaries would show small cystic degeneration that I have often advised examination of the patient and careful palpation of the ovaries, even under anesthesia, if necessary, and resection of the cystic organs, should they be present, which indeed they often were. Schroeder, for example, states that in many of his cases of hyperplasia of the endometrium, corpora lutea were lacking or subnormal, menorrhagia was not present, and even menstruation was decreased or absent. In such cases, of course, there would be a cumulative action of the follicular substance without the respite caused by menstruation, and therefore continued proliferation would take place. At the same time certain authors (Novak and others) found corpora lutea in the ovaries in most cases of endometrial hyperplasia. This also has been my usual experience. Whether or not we find corpora lutea does not make any difference in the underlying etiology, since the endometrium, even if lost at menstruation, can grow very fast, especially under the impulse of excessive follicular activity. I have seen a thin, dense endometrium completely covered by regenerated epithelium as early as the day after the cessation of menstruation.

In some cases of endometrial hyperplasia, menorrhagia occurs, whereas this is absent in others. This also is not a contradiction. I believe here that it depends on the amount of corpus luteum hormone carried by the blood supply to the particular part. Thus, as mentioned in a previous paper, the follicular action, because it may be continued for months and thus be cumulative, may be sufficient to cause endometrial hyperplasia while the corpus luteum action in the nature of things cannot be thus cumulative. It may be insufficient to cause the endometrial changes necessary as a preliminary to menstruation, so that externally at least no sign of corpus luteum activity will become evident.

Hammond has shown that in the ferret, which ovulates only on coitus, the same endometrial picture, the result of follicular activity, is carried through estrus, if coitus, and thus the formation of a corpus luteum, is prevented. That menorrhagia also occurs without hyperplasia of the endometrium is no contradiction since other not directly related causes may of course lead to uterine bleeding.

The small cystic degeneration of the ovaries used to be interpreted as due to inflammation, but this is certainly not so. It is due to congestion, and the increased blood supply causes an increased number of follicles to ripen, and this in turn causes the endometrial changes. The fact that endometrial hyperplasia is more frequent around the fortieth year of life, I believe we can explain by the fact that around that time many women are heavier, less active, and have perhaps a lessened muscular tonus, all of which causes would lead to pelvic congestion. In addition, I want to stress particularly constipation as a source of such congestion.

However, we have cases of endometrial hyperplasia where no evidence of ovarian hyperactivity and no small cystic degeneration of the gonads is present. I still believe we are dealing here with exactly the same process as before. More ovarian hormone may reach a particular area, first, because more of this substance is present in the blood stream, and second, because congestion and slowing of the blood current allows more hormone to seep out by a process of osmosis in one particular spot. Thus congestion would lead to hyperplasia, and uterine congestion is indeed often associated with endometrial hyperplasia. In some endometria, however, on one and the same slide different areas are seen which show different pictures of the menstrual cycle. Localized congestion or congenitally or otherwise abnormally situated or developed blood vessels and capillaries will explain just such an occurrence.

Since fibromyomas of the uterus grow only in the presence of the ovaries, and atrophy when these are lost, it seems perhaps not altogether unreasonable to interpret such tumors as being perhaps due to increased ovarian activity coupled to local areas of congestion, due to congenital or acquired formal defects or simply to stasis. If, on the other hand, there is diffuse congestion, it might cause the condition known as metropathia chronica. To me such an explanation seems more reasonable than Sampson's idea of irritation by retrograded menstrual blood. That the human female shows fibromyomata more frequently than other animals I would explain not by the fact that other mammals do not menstruate, but rather as being due to continued ovarian activity present in the human female—an ovarian activity by far the greatest and most consistent in the whole animal kingdom. The reason why there are so few fibromyomata of the tube and cervix is because these structures are normally incapable of reacting much to the ovarian hormone. Indeed, in accepting the theory of localized congestion and overactivity of the ovarian hormone, we may even assign a reason why the American negro is so frequently afflicted with fibromyomata uteri, while the aboriginal African black is not so afflicted. Anyone familiar with the strict rules of sexual abstinence of the aboriginal African blacks will certainly admit that these tribes are in comparison with the civilized American or European distinctly undersexed. There are also other reasons for thinking so, which I cannot take up here. I need only refer to the breast changes. Alfred Adler has called particular attention to the fact that organs below par are especially the ones which can and will react to a stimulus by an excessive reaction, and such excessive reaction may well, probably because of environment, food and living conditions, be accepted in the case of the American negro.



If we now turn to adenomyositis, we see that after the wolffian theory had been dropped more or less, and the serosal theory gained prominence, a why and wherefore of the lesions was sought. Robert Meyer thought he had found it in an inflammation of the area developing adenomyositic growths. It was thought that the inflammation produced loosening of the stroma and thus postfetal growth (Opitz, Pforte, Raspini, Schütze, Sitzenfrey, Vautrin, and others). Many cases indeed showed inflammation at the site of the adenomyositis and there can be no doubt that inflammation or irritation is a stimulus to growth; some of the pictures, especially Figs. 5 and 6 of my previous paper, illustrate this. It is also interesting in this connection that Spencer (*Gynecological Transaction* 50: 248, 1925) states that he never sees adenomyositis in laparotomy wounds, and thinks perhaps this is due to the fact that he carefully buries his sutures, whereas many American surgeons leave the suture ends fairly long, thus creating a source of irritation of the peritoneum. Although inflammation and irritation could be shown to be present in many adenomyositic lesions, other cases showed none at all, so that the name of adenomyosis was suggested by Frankl for the latter type of lesion. In every case of adenomyositis that I have observed there is, however, either clinically or histologically, an evident congestion present. I believe that this fact and not an inflammation per se is the crux of the matter. Lahm has seen cytogenic-like stroma develop in areas which showed convolutions and dilatation of the subserosal connective tissue of the uterus, either on the basis of congestion or due to certain formal defects in the tissue structure at this point, thus causing a relaxation of the blood vessels. Thus we may see adenomyositis at points where, for one reason or another, increased ovarian activity was applied, either because of increased follicular activity or because of localized congestion or, and most probably, because of both factors.

It might, of course, then be asked why we do not see adenomyositis in the acute inflammations of the pelvic organs or in chronic pyosalpinges, and why we do see invasion of the uterus by the endometrium, especially in older women. These objections I think are not serious. Acute inflammations often do not make their action felt for a sufficient length of time, and furthermore, all severe inflammations upset the whole organism so much and disturb the blood supply and lymphatics to such an extent, that locally applied ovarian activity does not occur. Indeed, in many of the severe inflammations the ovarian activity, together with the whole organic mechanism of the patient's body is depressed and not stimulated. That inflammation, however, often is the initial stimulus to heterotopic epithelial growth is shown by the frequency with which adhesions are found in such cases, and I believe that often such adhesions are primary and linked with the development of heterotopic endometrial growth, and are not secondary to it.

As far as invasion of the uterine wall by the endometrium, especially late in life, is concerned, we have, I believe, the same factors here at work that have been discussed under endometrial hyperplasia. Aside from this we may assume that the irregular corpus luteum production also has its effect, and that uterine muscle changes in addition may lead to changes in the tissue balance and allow of penetration of the endometrium. This to me is more logical than to assume, as has been done, that the basalis, in the course of the many years of its regeneration of endometrium, has acquired an activity which causes it to invade the uterine muscle because it no longer forms endometrium. The basalis, according to my observations, shares in the final atrophy upon loss of the ovarian activity, just as much as the rest of the uterine lining, and deficient ovarian function does not cause hyperplasia of the endometrium. I therefore consider Lauche's idea that the cause of adenomyositis lies in deficient ovarian function which gives rise to compensatory endometrial growth, as untenable. It could apply only if the endometrium had an hormonal activity similar to the ovary, and this has not been proved. In view of the dependence of endometrial growth on the ovary, and the loss of tissue each month from the uterine lining, I think this idea can be definitely considered to be illogical. Courier, because he found that injections of ovarian extract into newborn animals caused proliferation of vaginal epithelium, holds views similar to Lauche. Ovarian extract, however, causes not only vaginal but also the rest of the müllerian epithelium to grow. That Robert Meyer saw a "verschleimung" of the vaginal epithelium in bitches during pregnancy, also does not support Lauche's theory, since we are dealing here not so much with a deficient ovarian activity as with increased corpus luteum activity.

There is only one last point to consider, namely, the question as to why the lower parts of the pelvis and the ovaries are especially often the seat of adenomyositis. If congestion plays any rôle, naturally the lowest parts of the celom would be most frequently affected. The ovary is very prone to congestion and often prolapses. Adhesions also occur frequently. Again the blood and lymph vessels (and according to Bruhns there are only six or eight lymph vessels in the ovary) enter the hilus and then become very convoluted, thus further leading to congestion. In addition, it is probably true that nearer to the source the blood stream contains more ovarian hormone than further away.

In conclusion, I wish only to say that while the theory offered is necessarily purely hypothetical, certain clinical and pathologic evidence seems to support it. I believe it to be at any rate more logical than the "menstrual blood" conception of Sampson, for which reason I offer it here for what it may be worth.

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30 EAST FIFTY-EIGHTH STREET.

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D'Aprile, F.: Diabetes, Pregnancy and Insulin. La Clinica Ostetricia. 29: 353, 1927.

Only a few diabetics become pregnant. This sterility is thought to be relative only, being due to endometritis, imperfect ovulation and poor physical condition. If the diabetes is present before the onset of pregnancy it will be very much aggravated by the pregnancy. Its onset is very insidious and slow and results in a very grave condition toward the end of the pregnancy. In many cases a spontaneous abortion occurs and more frequently a premature labor.

Another common complication of pregnancy and diabetes is polyhydramnion. This is found in 20 per cent of the cases and is especially manifest in the grave cases. The total amount of amniotic fluid may be as high as twelve liters. The babies which are born prematurely often appear quite similar to the hereditary syphilitic babies. Weights as high as 7000 gm. have been reported.

There is always grave danger in allowing a diabetic to go through labor because of the lacerations and infections which may occur, since the diabetic is particularly prone to infections.

In patients who have had a definite diabetes mellitus and who have been treated with insulin during pregnancy, the babies have very often been stillborn. The insulin therapy may help the mother but has little effect upon the fetus.

J. M. PIERCE.

## GONORRHEA IN THE FEMALE\*

By LUCIUS E. BURCH, M.D., F.A.C.S., NASHVILLE, TENN.

*(From the Service Department Gynecology and Obstetrics, School of Medicine,  
Vanderbilt University)*

IT GIVES me great pleasure to lay before this learned society my results in the treatment of gonorrhea in the female. I have no apologies to offer for this commonplace subject as it is the most outstanding, unsolved problem that confronts our specialty today. My conclusions have been drawn from the first 100 patients treated in the Vanderbilt University Hospital according to the method that I will outline.

The cases reported in this paper all had positive smears. No case, however typical clinically, has been included if positive smears were not obtained. The series is somewhat unique in this respect and the good results are in my opinion, due to the fact that occasional cases of streptococcal or tubercular pelvic infection have been excluded.

The diagnosis of gonorrhea from smears at best is a laborious procedure, as only a third to one-half of those infected will show positive smears unless repeatedly examined. Diagnosis by means of culture has been tried, but results have been unsatisfactory. I am inclined to believe this is the ideal method, but for practical purposes it is yet an uncertain procedure.

The complement-fixation method has not been used on account of practical and physical conditions existing in the hospital. Repeated negative smears following the menstrual periods in absence of symptoms have been the criteria of cure.

There are three sites of infection in the female: the urethra, Bartholin's glands, and the cervix. It is not unusual to find all three sites involved. The one that is more likely to escape is Bartholin's glands, and the one that rarely, if ever escapes is the cervix. When the gonococcus obtains a foothold in the cervix it remains almost indefinitely, reinfecting the other two sites and what is still more disastrous traveling through the uterus over the endometrium to the tubes producing a salpingo-oophoritis and pelvic peritonitis with all of its disabling sequelae.

The vagina is only involved in children and young girls. The endometrium does not offer a fertile soil for the gonococcus except in puerperal cases. Gonococci are only found in the lower urethra. They do not ascend to the bladder, a neisserian infection of this organ being almost a medical curiosity. The infection in the urethra may be pri-

\*Read (by invitation) at the Fifty-fourth Annual Meeting of the American Gynecological Society, Old Point Comfort, Va., May 20-22, 1929.

mary or it may be secondarily involved from secretions from the cervix. The urethra offers a good resistance against gonococci and in due time will overcome them, unless reinfection takes place from the cervix or unless it is continually irritated by active treatment. Urethral symptoms as a rule are mild. In many cases they are barely noticed by the patient. In a few females with sensitive urethrae the symptoms may be quite prominent but even here they quickly subside unless badly managed.

Skene's ducts which are situated on the floor of the urethra and just inside the meatus are involved in only a small percentage of cases. They do not put up a good fight against the invaders and when infected they are likely to remain so for a long time.

Urethritis is best managed by a let-alone policy. Eradicate the other foci and nature will clear up the urethra. I desire to strongly condemn injection, irrigation, and topical applications. Hot sitz baths, urinary antiseptics and sedatives will make the patient more comfortable and assist nature in its natural resistance.

Skenitis on the other hand should be vigorously treated. It should be suspected in all cases of urethritis that do not clear up in a few weeks. The ducts are easily found if the meatus urinaris is dilated and a proper skenescope used. Occasionally the ducts can be seen without dilatation or the use of an instrument. Skenitis if looked for and recognized is easily eliminated. A cure is effected by laying open the ducts with a small cautery. Another easy and equally effective method is the injection of the ducts with tincture of iodine through a probe pointed needle.

Infection of Bartholin's glands is usually unilateral. It may be the first symptom that calls the attention of the patient to her infection and if not eradicated is likely to produce recurrent attacks. The most certain method of eradication is excision of the glands. This, however, is not always possible on account of abscess formation and rupture at the time the case comes under observation. Under these circumstances the abscess should be opened if this has not already occurred spontaneously, the cavity curetted, fulgurated and packed with gauze and made to heal from the bottom.

The cervix offers a problem which is well worthy of our deepest consideration. This is the favorite breeding ground of the gonococcus. From this site the infection may go up or down. If it goes up it will produce an infection of the appendages. If it goes down it will produce a reinfection of the urethra or Bartholin's glands. As long as the infection persists in the cervix, so long is it a menace to the woman's future health and happiness and so long is she a distributor of gonorrhea, should sexual relations take place.

The symptoms of cervicitis are mild unless associated with salpingitis, and under such circumstances the cervix is likely to be overlooked

by the attending physician. The only symptom of cervicitis is an increased leucorrheal discharge. This may be associated with a feeling of fullness in the pelvis and a low backache, due to uterosacral pathology. These symptoms are common in females and likely to be overlooked. I use the following surgical procedure for the relief of gonorrheal cervicitis:

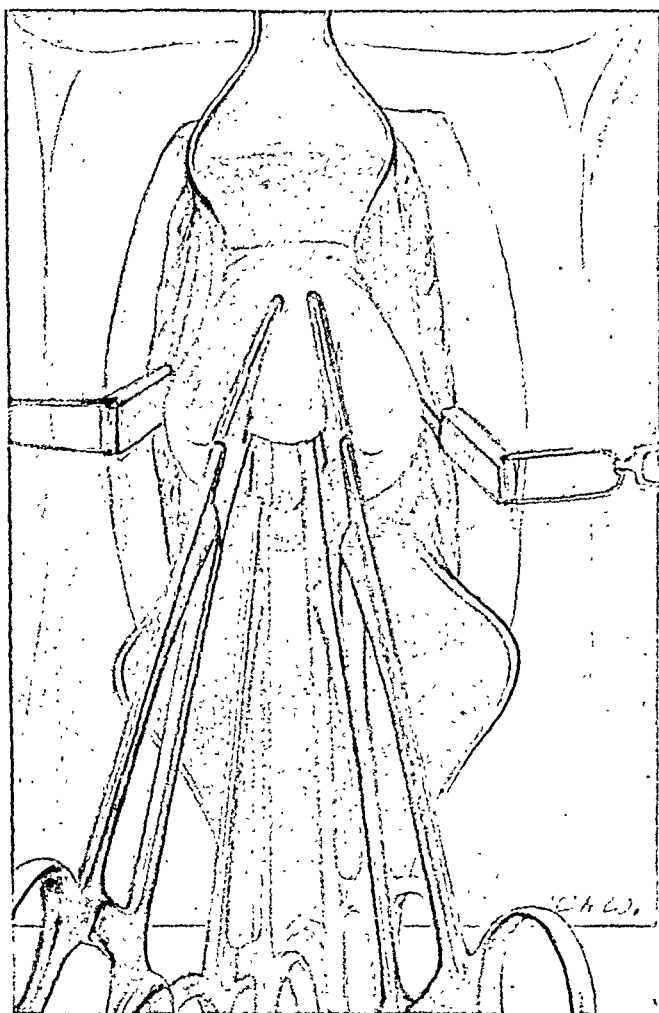


Fig. 1.—Cervix brought to vaginal outlet and forceps placed on each side of median line on anterior and posterior lips for purpose of hemostasis.

It should not be carried out at the height of an acute pelvic inflammation for fear of spreading the infection. It is also difficult at this time to expose and bring down the cervix while it is firmly fixed to the surrounding tissue. One can use satisfactorily sacral, general or spinocaine anesthesia. The cervix is exposed and steadied by volsella, and a hook as shown in the illustration is placed in each lateral lip. Any standard needle holder may be used to insert the hook. After insertion the needle holder is removed and traction is made by the chain. These hooks will not produce bleeding at the site of insertion nor will they pull out, and the view of the deeper parts is not obstructed by handles. The cervix is then dilated with Hegar's dilators (not Hank's), the dilatation being carried to at least size 12 and

occasionally to size 20. It is essential that the folds of the mucous membrane be flattened out by the dilatation in order to make the subsequent cauterization effective. Two artery forceps with blades sufficiently long and with not too strong a bite are placed on each side of the median line of the anterior and posterior lips for the purpose of complete hemostasis. The cervix is then opened up in the median line of the anterior and posterior lips to the internal os. The forceps on one-half of the cervix are spread in opposite directions and this brings in view one-

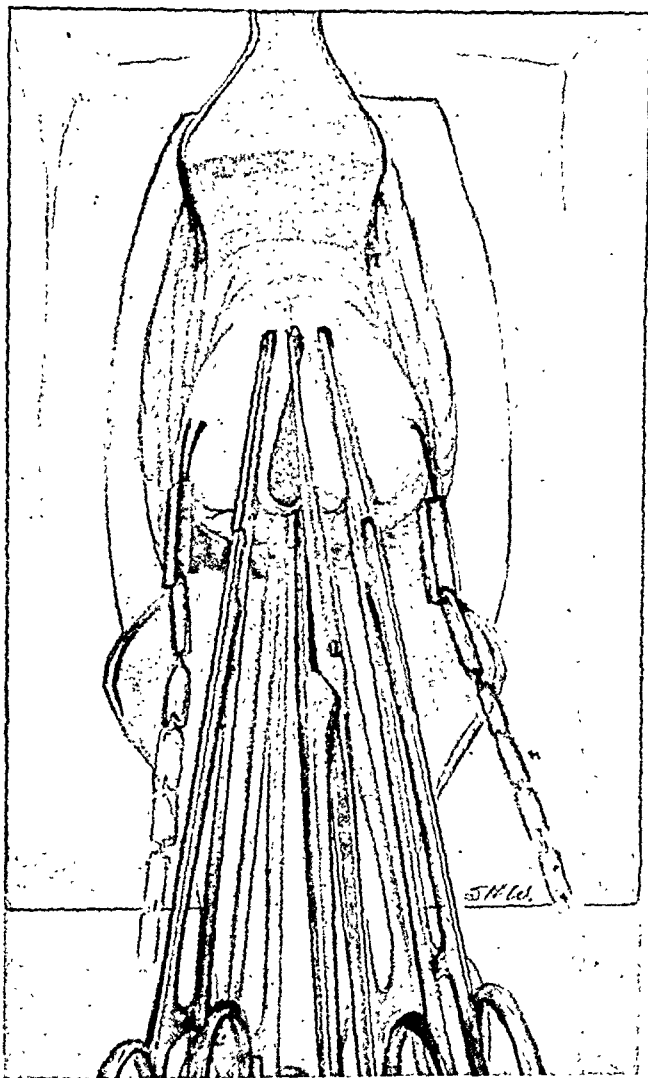


Fig. 2.—Incision of anterior lip of cervix to internal os with scissors.

half of the endocervix. The exposed area is then thoroughly cauterized and the same step carried out on the opposite side. The forceps are now removed and the area of mucous membrane that was in the bite of the forceps is cauterized. It is important that the cauterization be carried well up to the internal os. It is at this point that gonococci are quite difficult to eradicate and this explains why a Sturmdorff's operation often fails to cure a gonorrheal cervicitis. The incisions in the anterior and posterior lips are then closed with interrupted catgut sutures. The cervical canal is lightly packed with gauze. This gauze is removed at the end of

forty-eight hours and the parts are kept clean by sitz baths and pitcher douches. Unless there is some contraindication such as large pelvic masses, the patient is allowed to leave the hospital at the end of four or seven days, returning every week for smears for at least two months. Complete abstinence from alcohol and sexual relations must be practiced during this period. The most reliable smears will be those taken immediately following a monthly period. If the operation is properly performed the cervix will be cleared of gonococci and will remain so unless intercourse takes place with a partner harboring this infection.

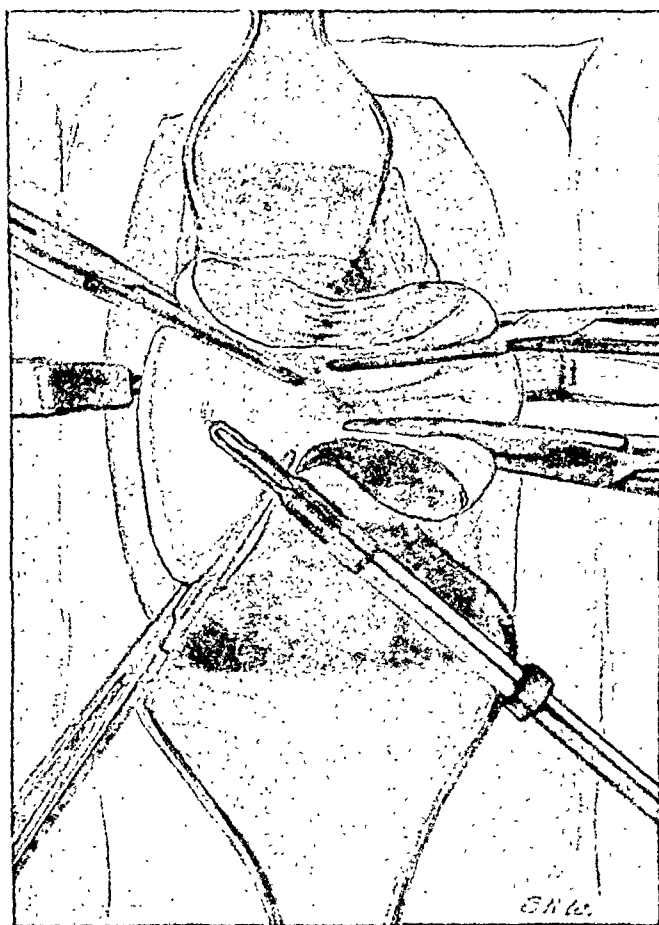


Fig. 3.—Cauterization of one side of endocervix. It is exposed by pulling hemostatic forceps on that side in opposite directions. I have used in a few cases the electrical coagulator with gratifying results. Time and experience may show that the coagulator is preferable to cautery.

Four of the patients in this series have been delivered. Two of the 4 had normal labor. One had labor induced at the eighth month on account of toxemia, the fourth had a shoulder presentation associated with a Bandl's ring and the delivery of a dead child. Two others to my knowledge are now in the early months of pregnancy. Five had slight hemorrhages ranging from seven to fourteen days after the operation on cervix. None of these hemorrhages have been alarming and not as severe as I have seen after linear cauterization. I have been



unable to find a single case that developed a stricture of the cervical canal.

For the relief of the epidemic form of vulvovaginitis in children I advise ointments, topical applications and vaccines. I want to strongly condemn the use of douches and injections on account of what happened to one patient on the service of Dr. Horton Casparis, Head of Department of Pediatrics, Vanderbilt University Hospital. An eight-year-old child was admitted with a gonorrheal vulvovaginitis. The

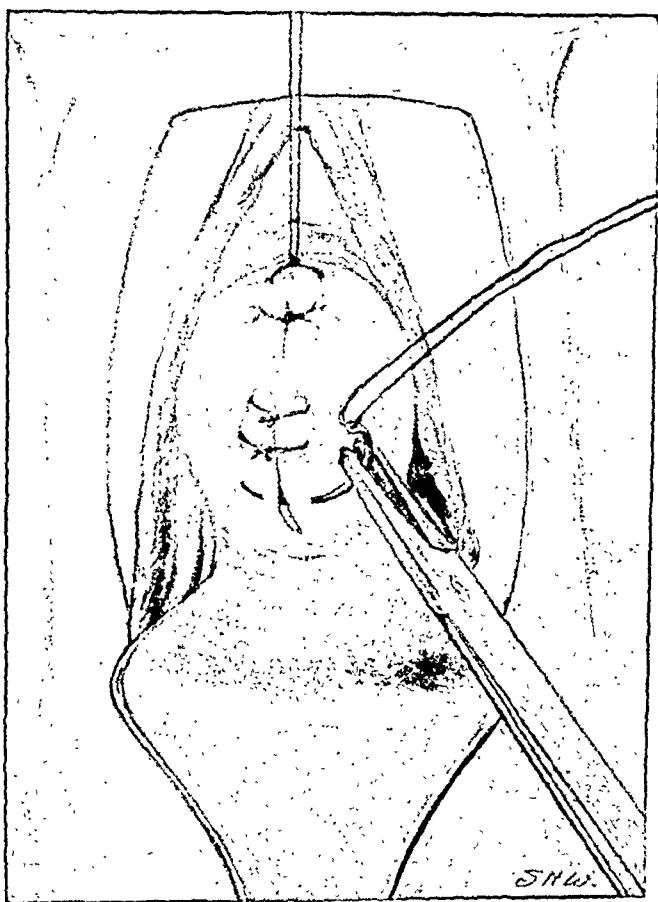


Fig. 4.—Closure of incisions in cervix with interrupted sutures.

treatment was instillation of mercurochrome in the vagina. She developed a general peritonitis and died. Postmortem showed mercurochrome all over the peritoneal cavity.

Many patients are unaware of their trouble until the disease reaches the tubes, ovaries, and pelvic peritoneum. The well-known symptoms of pelvic inflammation appear. Fortunately these tissues soon overcome the infection and the patient then believes she is well until another attack takes place. This will often happen unless the focus of infection is eliminated in the cervix.

I have been impressed many times in the past by the almost miraculous way in which nature handled pelvic inflammation. I have had several cases showing large masses in the pelvis in which I operated years afterward for other conditions and found the pelvic organs practically normal. Patients for whom operation had been advised and refused, later conceived through the same tubes that I had wanted to remove. These experiences lead me to the conclusion that nature assisted by rest, protein therapy, and other forms of palliative treatment would cause the pelvic inflammation to subside and if the focus of infection in the cervix was eliminated the patient would recover and remain well in the great majority of cases.

Palliative treatment for this condition is nothing new. It has a few advocates in this country and has been extensively used in Germany. The weak link in the chain in palliative treatment in the past has been the nonelimination of the focus of infection. It is now the custom in most American hospitals to treat all patients in a palliative way until acute symptoms subside and then to open the abdomen and remove all or a great part of the internal organs of generation. The net results of such surgery are that these young women lose their ovaries but are left with a cervical gonorrhea.

Of the 100 patients in this series not one has had an abdominal section and many of them had large masses that were the accumulation of several attacks of pelvic inflammation. Abdominal section has not been performed on a single patient with pelvic infection of gonorrheal origin in the Vanderbilt Hospital since it was opened in September, 1925.

It is hardly necessary to state that if a pelvic abscess forms it should be drained. Abdominal section is only indicated in those patients who have disabling masses in the pelvis which prevent them from following their ordinary routine of life, repeated negative smears and a sedimentation time of one hundred minutes or more. I consider the sedimentation test a most reliable one. It is not only a good index as to the progress of the infection but also is a reliable guide as to a safe time for abdominal section.

The total number of patients receiving milk injections was 66. The total number of milk injections was 301 and the average number of injections per patient was 4.56 plus. I strongly endorse the suggestion made by Polak of producing temporary amenorrhea with x-ray in this class of patients. This prevents the monthly congestion of the generative organs and gives nature a better opportunity to clear up inflammatory exudates. Some patients naturally have a soreness and tenderness in the parts for some time, but all of this will pass off in the great majority of cases if the focus of infection in the cervix has been eliminated.

Living in a city where the medical profession is on most friendly terms I have been able to follow those patients who later entered other hospitals. Five women who received this treatment in the Vanderbilt Hospital again contracted gonorrhea through illicit intercourse or mar-

riage. These patients were sectioned in other hospitals and a part or the whole of their internal organs of generation were removed. In 3 of the patients I was able to obtain the specimen removed at operation and in 2 others a report on conditions found in the pelvis was obtained from the operating surgeons. In none were large masses removed and I am firmly convinced that they could have been saved if foci of infection had been eliminated. I also have the report on 3 patients who had large pelvic masses at the time the cervix was operated upon and who were subsequently operated upon for appendicitis. In these 3 patients the operating surgeons reported that the pelvic organs were normal or almost so. For the woman who is mentally and morally deficient and who will immediately take chances on reinfection, I can offer no solution for the problem. For the woman who wants to get well and remain so I can recommend the treatment outlined. It will cure the gonorrhea and will make abdominal section unnecessary in over 90 per cent of cases.

(For discussion, see page 732.)

## AMENORRHEA DURING SERIAL ROENTGEN EXPOSURES DUE TO INTERVENING PREGNANCY

BY LEOPOLD GOLDSTEIN, M.D., AND DOUGLAS P. MURPHY, M.D.,  
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(From the Gyneccean Hospital Institute of Gynecologic Research, University of Pennsylvania)

**N**ORMAL menstruation and pathologic uterine hemorrhage may be diminished or suppressed by pelvic roentgen therapy. A subsequent amenorrhea is usually attributed to the irradiation, though this may not be the cause. For instance, conception may have taken place just prior to treatment, which may not be suspected at the time of roentgen exposures. In addition, it is quite possible that the amenorrhea, occurring after one or more of the roentgen treatments, may be due to an intervening pregnancy. An assumption that the amenorrhea is due to the irradiation may allow the gestation to proceed unrecognized, as long as abortion does not occur. If conception takes place during or immediately before a series of roentgen exposures, the result may be a very early exposure of the embryo, which may thus receive a large amount of irradiation.

In a recent study of the health of children born after maternal pelvic radiotherapy,<sup>7, 8</sup> it was concluded that postconception irradiation seriously interferes with fetal development. Mental retardation, manifested by microcephalic idiocy, was frequently observed in the children irradiated in utero, 24 per cent of the cases, to be exact.

As the basis of this paper we have used the reports secured from the current literature, upon 12 women who became pregnant in the interval between roentgen treatments. Brief extracts of these reports are recorded in the table. It will be observed that several women received a large number of roentgen exposures during pregnancy. Three of them gave birth to microcephalic idiots, whereas eight of them bore healthy children.

This report emphasizes the fact that conception, occurring before or during a series of roentgen exposures, may remain unsuspected throughout the entire course of treatment. Pelvic irradiation during pregnancy is prone to be extremely detrimental to the embryo. It is, therefore, exceedingly important to know the physiologic state of the uterus before pelvic roentgen treatment is instituted.

TABLE I. PREGNANCIES BEGINNING DURING INTERTREATMENT PERIODS

AUTHOR	TIME OF CONCEPTION	CONDITION OF CHILD
Apert, E., and Kermorgant	Coincident with amenorrhea after the first of 17 treatments	Microcephaly
Edelberg, H.	During the third month of treatment	Normal
Eymer, H.	Between treatments	Normal
Falkenheim, H.	Between the first and second treatments	Microcephaly
Foveau de Courmelles, V.	Between treatments	Stillborn
Ménard, M.	Between two of the eight treatments	Normal
Ménard, M.	Between the seventh and eighth of a series of 18 treatments	Normal
Ménard, M.	Between the 29th and 30th of a series of 35 treatments	Normal
Naujoks, H.	Between the first and second treatments	Microcephaly
Rénon, L., and Degrais	Between treatments	Normal
Schmitt, W.	Between treatments	Normal
Werner, P.	Between treatments	Normal

Norris<sup>11</sup> is a firm advocate of curettage preliminary to the employment of any pelvic radiotherapy. This procedure eliminates the possibility of unwittingly irradiating an embryo and, by histologic examination of the curettings, the condition of the endometrium is determined with certainty. In older women, among whom pathologic hemorrhages are common, the diagnostic curettage prevents the possibility of overlooking a carcinoma of the fundus, which is especially likely to escape notice if a myoma is present. In 75 per cent of the unsuspected fundal carcinomas occurring in the John G. Clark Gynecologic Clinic at the University of Pennsylvania, the symptoms of the malignant neoplasms were masked by preexisting myomas.

If a series of roentgen exposures involving the lower abdomen or pelvis is contemplated, the patient should not be permitted to become pregnant while the treatments are given. For several months after

the completion of the exposures, the patient should be watched for evidence of a conception having taken place in the interval between any two of the last several treatments. If pregnancy is found, abortion should be induced at the earliest possible moment, so as to prevent the birth of a defective child.

#### CONCLUSIONS

1. The amenorrhea concurrent with a series of therapeutic roentgen exposures may be due to pregnancy.

2. Conception may take place immediately before the first of a series of roentgen exposures, or may occur in the interval between any two of them.

3. An embryo may be damaged by maternal pelvic irradiation and consequently develop into a mentally defective child.

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Maternal obstetric sciatic paralysis occurs only rarely. It usually follows a severe labor in which decided difference between the size and shape of the pelvis and that of the fetal head is encountered, and in which more or less extensive instrumentation has been employed. The paralysis is apparently due to an increase in the intrapelvic pressure causing trauma to the sciatic nerves. The symptoms usually appear immediately after delivery, but are at times delayed several days. They are bilateral and include motor and sensory changes. Drop foot resulting from involvement of the external perineal nerve is a conspicuous sign. It may disappear partially or completely, but at times remains permanently. The treatment is entirely symptomatic, and the prognosis must be guarded, for we have no means of discerning the degree of trauma to the sciatic nerves, nor do we know any curative measure.

WILLIAM C. HENSKE.

# Society Transactions

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## THE AMERICAN GYNECOLOGICAL SOCIETY

### FIFTY-FOURTH ANNUAL MEETING

OLD POINT COMFORT, VA.

*May 20, 21 and 22, 1929*

The papers presented at this meeting were as follows. For lack of space, the discussions necessarily must be presented in abstract.

**Acute Puerperal Inversion of the Uterus**, by DR. PALMER FINDLEY, Omaha, Nebraska. (For original article, see October issue, page 587.)

### DISCUSSION

DR. B. P. WATSON, NEW YORK, N. Y.—This is a rare condition and none of us can have any large personal experience with acute cases. There is not a single case in the Sloane Hospital for Women records between 1921 and 1929, during which time over 13,000 patients have been delivered. I, personally, have seen only one case of acute inversion and operated on three cases of chronic inversion. None of them had been recognized at the time of labor. One case was rather remarkable.

The patient had a normal labor, but there was some slight delay in the expulsion of the placenta. A slight dimpling in the uterine fundus after expulsion of the placenta was noticed, but the fundus was palpable through the abdomen. The patient began to run a temperature immediately, and by the third day she was acutely ill with a temperature of 105°. Cultures from the vagina and from the blood were positive for hemolytic streptococcus. The course was very stormy for the next ten days when temperature was falling, blood culture had become negative and she looked better. Vaginal examination was then made and the inverted fundus felt in the vagina. It was obviously unwise to do anything at that stage. Three months later I operated by the abdominal route. The ring was incised posteriorly and the uterus reinverted. The peritoneal surface of the reinverted uterus was found covered with shaggy adhesions and I deemed it wise to do a supravaginal hysterectomy.

One of the other cases had a somewhat similar history. She was delivered in one of the city hospitals in Edinburgh, and had run a septic temperature in the puerperium. Patient was examined at the end of three weeks when inversion was discovered. In this case also, after an interval I reinverted by the abdominal route. The pelvis in this case was quite free from adhesions, and we left her with a functioning uterus.

In cases of acute inversion treatment of shock before attempting reposition is most important. An acute inversion is in the nature of an acute abdominal lesion, and the shock may be profound.

DR. HARVEY B. MATTHEWS, BROOKLYN, N. Y.—At the Methodist Episcopal Hospital we had four cases of acute inversion in about 17,000 deliveries. Strange to say these four cases happened in two consecutive years, viz. 1925 and 1926. I think there are two reasons for this: first, we had a house officer who persisted in manipulating the fundus and otherwise interfering with the normal

mechanism of the third stage of labor; and second, we were using an ampule of pituitrin before the placenta was delivered with an ampule of gynergin or aseptic ergot after its delivery.

According to G. H. Davis, we have to recognize two kinds of acute inversion: acute spontaneous and acute delayed. The acute spontaneous inversion one naturally treats with reposition. In two of our cases we did this under surgical anesthesia, packing the uterine cavity with 4 per cent mercurochrome gauze. Both patients did well and went home at the usual time.

The other two cases fall under the classification of spontaneous delayed inversion. They were not recognized for ten days in one instance and twelve days in the other. We believe that in these two cases the inversion was gradually taking place during the ten and twelve days and was caused by a flabby and atonic uterus and overdoses of oxytocic drugs, e.g., pituitrin, ergot, etc. One case had three ampules of pituitrin and one of aseptic ergot after the placenta was delivered. These two cases died of shock and hemorrhage without reposition shortly after the accident. We do not (as Dr. Findley advised) attempt reposition until the patient recovers completely from shock.

The advice to do an immediate abdominal section and reduce the inversion from above seems to us too radical a procedure. An inversion which can be reduced from above, it seems to me, can be reduced as well from below. Deep surgical anesthesia, gentle manipulation and plenty of time are important prerequisites. Abdominal section on an already "shocked" patient is hazardous.

DR. G. BROWN MILLER, WASHINGTON, D. C.—I have to acknowledge three cases of uterine inversion in my private practice. One occurred without any manipulation of the fundus or pulling on the cord in a multiparous woman with a relaxed vaginal outlet. A few minutes after the child was expelled she had a tremendous pain and the placenta attached to the completely inverted uterus shot out of the vagina.

The other two cases were due no doubt to too vigorous manipulation of the uterine fundus where the woman was having considerable bleeding.

There was no very excessive hemorrhage in any of the three cases. There was no shock that could not be accounted for by the bleeding. In every case the treatment was the same. We used gauze to separate the placenta, irrigated with normal salt solution, and then adopted a method which I believe is of great value. The trouble in reinversion of the uterus is that attempts to reinvert it may fail because there is nothing to push against, as it were. In every case we gave the patient anesthesia, pushed the whole mass as far upward as possible until the vagina was put upon a stretch, and during a relaxation of the uterus the manipulation of reinverting it in the exactly opposite way from which it became inverted was followed, and we had no difficulty. In no case was there rise in temperature above 100° or subsequent infection of any kind. After I was assured the uterus had been reinverted, the patient was given some pituitrin and was watched for several hours. Packing was not done in any case and in none of the three cases was there any subsequent inversion.

With good technic I believe there is no more danger to the woman with a complete inversion *promptly recognized*, and *properly managed* than in detaching an adherent placenta by means of the hand in the uterus.

DR. JOSEPH P. DELEE, CHICAGO, ILL.—I would like to ask the chair to have each gentleman give the number of cases of inversion that have come under his notice that have not been published. That would give us a cross-section of the experience of the country as a whole. In something over 65,000 labors in the Chicago Lying-in Hospital there is only one case of total inversion of the uterus reported.

During the last five years we have given pituitrin routinely after the baby is born and have had only this one inversion, so I doubt if the pituitrin can be incriminated. In two of my cases the uterus began to turn inside out as I was watching the third stage. I reinverted the fundus of the uterus very quickly and packed. Had I been less watchful these cases would undoubtedly have had to be recorded as complete inversions.

I did a cesarean section on a woman who had an inverted uterus in a previous labor where Spinelli's operation had been performed. She had had a stormy recovery but lived to have her second child. At the subsequent cesarean I found a very thin scar.

The case mentioned first was attended by an intern who was very nonchalant; when the uterus turned inside out, he simply pushed it back again as though nothing had happened, and the woman made a complete recovery.

Since then a patient died in her home before she could be brought to our hospital.

DR. JOHN O. POLAK, BROOKLYN, N. Y.—Statistics are absolutely unreliable because there is no question that the incidence of inversion is much greater than appears from recorded instances. In 17,000 cases that we have had in our service there has not been a single case of inversion and yet in my personal experience I have seen six cases, none of which has been reported. The first one was the most appalling and happened 30 odd years ago in a tenement house. There was no hemorrhage but the shock was severe. We infused this woman with a saline solution, gave her morphia, and she recovered from the shock promptly.

There is one point I would like to make in regard to the use of anesthesia and that is there is no anesthetic that will relax the cervix so perfectly as chloroform. Gas or ether will not do it.

I take the stand with Dr. Findley that the vaginal procedure of reposition is the safer one because in the cases we have seen so far we have not lost any and have operated by the vaginal method. In two cases where we could not relax the cervix, we have split the cervix, reinverted the uterus through the enlarged ring, and followed with firm packing.

Another point which must be emphasized in regard to hemorrhage is that whether it be placenta previa or inversion, these patients will not stand any operative procedure unless they are previously transfused.

DR. F. C. IRVING, BOSTON, MASS.—Dr. Huntington, Dr. Kellogg, and myself have had six cases of inversion. They have all been treated by abdominal operation, and all six have recovered. The time when operation was instituted following the appearance of inversion varied from one-half an hour to twelve hours. In three of these cases previous attempts had been made to reduce the inversion from below, but the hemorrhage was so severe and the attempt so fruitless that it was abandoned. All cases were transfused at the time the operation was started.

The operation as we have done it is not very complicated. All we do is to open the abdomen in the midline, the inversion presents itself, and the operator and his assistant reach down, grasp the uterus with forceps and both pull at the same time. They reduce the inversion in the reverse order from which it went down so that it is like putting a stocking on wrong side out and pulling it over your foot. We have seen no shock whatever. As a matter of fact, the patients come out of their previous shock as soon as the uterus is reinverted.

DR. BARTON COOKE HIRST, PHILADELPHIA, PA.—I have had six cases of inversion of the uterus; three were reduced by taxis and three by Spinelli's operation. It is not to report these cases but to record an observation that is very unusual that I take part in this discussion.



My predecessor, Dr. Penrose, one of the founders of this Society, said he was consulted by a farmer's wife in Pennsylvania who had a complete inversion of the uterus for which he proposed the application of weight, which many used in those days. The woman refused treatment, returned to Philadelphia a year later, and to his great astonishment he found her three months' pregnant with a spontaneous correction of the inverted uterus.

DR. FREDERICK C. HOLDEN, NEW YORK, N. Y.—There were three cases of puerperal inversion of the uterus admitted to the Gynecological Department of Bellevue Hospital during a period of nine months, which present points that may add to the interest of Dr. Findley's paper.

CASE 1.—Immediately after the third stage of labor patient had a severe hemorrhage, went into shock and was transfused. No vaginal examination was made before her discharge on the eighth day postpartum. She had two normal menstrual periods, but following the latter she had a severe hemorrhage and was transfused at the Jersey City Hospital. Upon examination they found an inverted uterus which they were unable to reduce. Patient was admitted to Bellevue Hospital where the diagnosis of complete inversion was confirmed. After two weeks of high elevated foot posture and hot saline douches the uterus spontaneously replaced itself, and she was discharged recovered.

CASE 2.—Patient had inversion following forceful Credé at which time she was transfused. Admitted to Bellevue with complete inversion. The condition was not benefited by posture and douches, and uterus could not be replaced under full ether anesthesia. A Spinelli operation was performed, pre- and postoperative transfusions were given, anterior and posterior culdesacs were drained. She recovered after a somewhat stormy course. One and a half years later she was admitted to the obstetrical service in active labor. Following the spontaneous delivery of a full-term breech she went into profound shock, diagnosis of ruptured uterus was made, and a rapid supracervical hysterectomy was done with pre- and postoperative transfusions. The abdominal condition remained excellent, but she developed a bronchopneumonia from which she died one week later.

CASE 3.—Primipara, aged 16, admitted very anemic three weeks after a home delivery. Complete inversion of the uterus, not reducible by several weeks of posture and hot douches, nor under full anesthesia. Spinelli operation was done, with drainage of anterior and posterior culdesacs and pre- and postoperative transfusions, followed by a smooth convalescence and good recovery. Normal menstruation since.

Comment.—Pregnancy following Spinelli operation should be terminated by an elective abdominal section.

DR. F. L. ADAIR, MINNEAPOLIS, MINN.—We have had two cases of acute puerperal inversion in the Minneapolis General Hospital, and both patients died.

CASE 1.—I saw the patient only after the uterus had been replaced. Patient was a primipara, 28 years old, admitted on April 26, 1925, two hours after membranes had ruptured. Only slight pains during the day and no progress was made. Floating head until April 27. Patient was delivered at 7:10 P.M. on April 27. Prior to delivery the cervix showed at the vulva. Following delivery, the uterus was firm, about one finger below the navel; very slight bleeding. Placenta seemed to be attached to the fundus. There was a slight dimpling in the center of the fundus where the placenta seemed to be attached. The placenta came down after twenty-five minutes, with slight pressure from above. No Credé was used. The placenta lay in the vagina and was gradually and carefully pulled out, but seemed

attached, and when it emerged from the vagina was followed by a large cone-shaped mass of blood oozing from its surface. No uterine corpus could be felt in the lower abdomen. This mass was replaced but came down slightly and was again replaced. Patient bled rather freely, but her condition was fairly good, pulse 104-130. Further interference was not advised, supportive treatment was given with fluids and transfusions; also  $\frac{1}{2}$  c.c. of pituitrin and ergot was given hypodermically. There was a first degree tear of the perineum. Total blood loss was about 1000 c.c. Patient returned to bed and condition became worse, and in spite of stimulants and hypodermoclysis, she died while being transfused about three hours after delivery of the placenta. Total duration of labor about thirty-four hours. Baby survived in good condition.

CASE 2.—This case is the only one I have ever seen with the uterus inverted. Patient, aged 29, grav. vii, para v., admitted December 23, 1928. Pregnancy at term, in labor. All previous deliveries were spontaneous. This pregnancy normal throughout. Patient started to have pains at 1:30 A.M. December 22. Pains continued for about five hours, stopped and began again at 6:00 P.M. At time of admission, 12:30 A.M., December 23, pains were coming about every twenty minutes. Later patient had severe labor pains at intervals of eight to ten minutes for about twelve hours with slow progress. Pains then came closer together but still no progress, so she was given rest with morphine and magnesium sulphate. A diagnosis of L.O.P. position was confirmed by x-ray examination. Patient continued to make little progress and became very much exhausted. At 10 P.M. dilatation and effacement were complete, and then because of the posterior position and maternal exhaustion a version and breech extraction were done. A normal female infant weighing 4258 gm. was delivered at 10:55 P.M., with no perineal lacerations. Placenta was delivered easily with no traction on cord and only slight pressure on fundus at 11:12 P.M. Blood loss at delivery was 350 c.c. Condition of patient immediately after delivery was good. A small hemorrhage occurred when patient was being moved from delivery table. The uterus was gently massaged and pituitrin 0.5 c.c. was given and later repeated. At 11:50 P.M., 55 minutes after delivery, patient began to have profuse vaginal hemorrhage and called to the nurse that she had passed something. On immediate examination the uterus was found to be completely inverted, lying between her thighs, and bleeding profusely. Patient was in severe shock. Blood pressure was about 70 systolic, pulse not perceptible at wrist; extreme restlessness and pallor were noticeable. External heat was applied, morphine sulphate gr.  $\frac{1}{6}$  given and intravenous saline started at once. An attempt to replace the uterus was unsuccessful, so hot sterile saline packs were applied to control the hemorrhage, and 1000 c.c. normal saline given. Pulse became better in quality. Patient complained of severe pain in abdomen with desire to bear down. She was then taken to surgical department and uterus replaced and packed. Condition was critical at this time. Death certified at 1:25 P.M., two and a half hours after delivery. Autopsy diagnosis: Postpartum inversion of uterus with hemorrhage and shock, clinical. Very mild bronchopneumonia. Unexplained toxic changes in liver, spleen, and kidneys. Obesity. Streptococcic septicemia. Culture of spleen showed streptococcus. Examination of the uterus showed an apparently relaxed lower segment.

There has been some mention of degeneration of the uterine muscle as a predisposing cause. Microscopic examination was made of this muscle, and the muscle and fibers were found absolutely normal; the fat stain revealed no evidence of degeneration.

DR. JOSEPH BRETTAUER, NEW YORK, N. Y.—In view of the seriousness of this complication, I would like to call the attention of teachers in medical schools and in training schools for nurses, to the importance of instruction in the proper

care of the patient during the third stage of labor. It is surprising to those who have witnessed the energy employed by young assistants and nurses in handling the fundus during the third stage, that this condition has not occurred more frequently.

DR. E. L. KING, NEW ORLEANS, LA.—I saw an inversion in a case of placenta previa. The patient was moribund. The uterus was easily replaced but the patient died shortly afterward.

I know of two other cases of inversion occurring in private homes, one in the practice of my brother, who has delivered about 3,500 patients, and the other in the practice of a physician of less experience. Both uteri were manually replaced at once, and both patients recovered.

DR. L. A. CALKINS, UNIVERSITY, VA.—I would like to report one case of what we thought was inversion of the uterus, in view of its value from a differential diagnostic viewpoint. This woman was admitted to the University of Virginia Clinic approximately a year after an incomplete abortion which had been treated by curettage. She had a large mass protruding into the vagina and covered with a very thick endometrium. Diagnosis of inversion was made and vaginal reposition attempt failed. Examination by laparotomy, however, revealed a hernia, posterior to uterus and down into the vagina. There was a loop of intestine caught in this hernia, but the woman had no signs of intestinal obstruction. We were rather ashamed of our diagnosis, but in view of these reports this morning I think it worth while to report this case as a point in differential diagnosis.

DR. CHARLES C. NORRIS, PHILADELPHIA, PA.—I would like to place on record a case which is perhaps a little different from those reviewed this morning. The patient was a very stout individual who had been delivered by high forceps six months before I saw her. She was sent to me with a diagnosis of submucous myoma and this was the superficial appearance of the tumor-like mass which presented from the vagina. Bimanual examination was unsatisfactory on account of the extreme thickness of the abdominal wall; however, on deep palpation what appeared to be a small uterus could be felt; no cupping could be detected. On account of the size of the uterus and history of the case an inversion was suspected, and the diagnosis verified under anesthesia. The fundus resembled Dr. Findley's specimen but was considerably smaller. It was impossible to replace, and a vaginal hysterectomy was performed with a successful result.

DR. ALEXANDER M. CAMPBELL, GRAND RAPIDS, MICH.—I would like to report a case of puerperal inversion of the uterus in which I attempted the Spinelli operation on the fifth day. I found in this case that this procedure was mechanically impossible and instead did a rapid supravaginal hysterectomy using a continuous circumferential suture to control the hemorrhage. Following the operation a direct blood transfusion was performed, and the patient recovered after a prolonged and stormy convalescence.

I agree with one of the previous speakers who remarked that the Spinelli operation is not always easy to carry out.

**A Preliminary Report on Temporary Roentgen Castration in the Treatment of Subacute Pelvic Inflammation**, by DR. JOHN O. POLAK, Brooklyn, N. Y. (For original article, see October issue, page 580.)

#### DISCUSSION

DR. C. F. BURNAM, BALTIMORE, MD.—Many gonorrheal inflammatory cases, as well as puerperal infections, light up at each menstrual period and, at that time,

the pain of the so-called endometriosis inflammatory disease is much exaggerated while often not present at any other time. It is well established that in inflammatory cases intrauterine radium treatment is dangerous, and the same can be said of full doses of x-ray.

It should be borne clearly in mind, however, that by the use of a fractional dose method it is possible, in inflammatory trouble, to produce an amenorrhea without stirring up the infection. As a rule, a period of amenorrhea, whether the inflammatory condition be of neisserian, tuberculous, endometriosal or streptococcal origin, is accompanied by subsidence of symptoms and improvements in the condition.

In addition to a beneficial effect from bringing on amenorrhea, x-ray application in proper dosage has a pronounced healing effect on tuberculous lesions, particularly on tuberculous salpingitis and peritonitis.

DR. JOHN A. McGLINN, PHILADELPHIA, PA.—It seems to me that with our modern treatment of acute pelvic inflammatory disease and the results which we obtain by rest and the treatment which Dr. Polak has already outlined, to introduce an added treatment which brings so much risk as irradiation, is unwise.

I have one patient under my care at the present time who had a very small dose of x-ray ten years ago, and she has never menstruated since.

It has been my experience to handle a number of cases after radiologists had treated them for hemorrhage, and I have had to operate frequently as a result of the lighting up of an old infection by their treatment. Furthermore, in many of the cases of sepsis if left alone the patients will recover and may bear subsequent children. While we cannot say just what effect radiation may have on the offspring as a result of preconception radiation, nevertheless, there is enough in the literature to show that this is a rather dangerous thing at times for the offspring.

Before adopting this measure all these things should be thought of: The possibility of sterilization, of stirring up the infection, and the possibility of an effect on the fetus from preconception radiation.

DR. CHARLES C. NORRIS, PHILADELPHIA, PA.—Irradiation has been employed in certain of the German clinics for these cases for some time. In our own clinic at the University of Pennsylvania we have felt that irradiation was somewhat hazardous in that it was prone to produce an exacerbation of the intra-peritoneal infection, and a history or palpable findings of an inflammatory disease is, therefore, with us a contraindication to this form of treatment. On the other hand, we have employed irradiation in some 600 or 700 patients suffering from benign hemorrhage with only three in which a reaction occurred. It is certain that some of these cases had an unsuspected salpingitis associated with the myoma, or other lesions.

If the adnexal lesions are sterile, as they will be in nearly all cases, if they have been quiescent for a period of a month or more prior to operation, the irradiation is harmless. If, however, the tubes and ovaries harbor virulent organisms, a flare-up is likely to result. In the ordinary dosage neither x-ray nor radium are sterilizing in their action. Certainly intrauterine irradiation by radium preceded as it usually is by a curettage would be more prone to cause an exacerbation than would the x-ray therapy.

If my assumption is correct that irradiation is harmless when the tubal contents are sterile, but is prone to produce an exacerbation when this is not the case, this will explain why a long series of myomata may be treated by irradiation without the production of a reaction. However, the difficulty in the employment of irradiation for cases of pelvic inflammatory disease is that it is impossible always to determine this point.

With the tubercle bacillus the problem may be somewhat different. X-ray therapy has been employed in the treatment of tuberculous peritonitis with more or less success in many recorded series of cases. The theory has been advanced in regard to these cases that whereas the rays are not destructive to the organism, stimulation of connective tissue occurs and tends to wall off and inhibit the offending microorganism.

For the reasons already stated I believe we should employ x-ray therapy with extreme caution in all cases of pelvic inflammatory disease and then only after other and less hazardous methods have proved ineffectual.

DR. HARVEY B. MATTHEWS, BROOKLYN, N. Y.—During an enforced stay in the Adirondacks a few years ago, I noticed that women who had pulmonary tuberculosis (patients in sanatorium) would have a rise in temperature every 28 to 35 days. One could follow the menstrual cycle by studying the temperature charts of these patients. It occurred to me that if temporary sterilization was done on these women the temperature would not rise periodically.

It was with a great deal of difficulty that I persuaded the authorities to try out this idea. Finally a few cases were treated in this way by the x-ray, and, as we suspected, no rise in temperature was noticed during the expected menstrual period. Everything else being equal, the temperature of a female patient with pulmonary tuberculosis does not rise quite as high as when she is menstruating, so that evidently there is something in the act of menstruating that produces this rise in temperature. Reasoning by analogy, the chronic inflammation case should react in the same way.

DR. JOSEPH L. BAER, CHICAGO, ILL.—Radiation therapy can cause devitalization of tissue, a result that should militate against its use in this connection. Those of you who have seen the magnificent Cinti film must be convinced that radiation has a definite effect on the vitality of tissues. The way in which the motion of the normal cell structures is gradually and completely suppressed by radiation and the destruction of the cellular elements in the malignancy picture under the microscope are a dramatic and ocular demonstration of the destructive power of radiation on cell vitality. With that thought in mind I agree with those who warn against too ready an adoption of temporary x-ray sterilization as an aid in the treatment of pelvic inflammation.

DR. GEORGE H. NOBLE, ATLANTA, GA.—We know the effect of x-ray on menstruation, but do not know in what way it acts, whether by destroying the germ cells or atrophying the ovaries and uterus, nor do we know of any undoubted effect upon the fetus of subsequent pregnancies. It has not been definitely shown that irradiation may affect subsequent offspring.

DR. JOHN O. POLAK, BROOKLYN, N. Y. (closing).—I think we should not be confused by the discussions we have listened to relative to radium versus x-ray or by the remarks of my friend, Dr. Baer, who has been showing us what x-ray will do in the destruction of cells. There is no question that radium will light up trouble and that x-ray given in sufficient doses will do exactly what he has said. I have presented this as the result of a clinical study that has helped us to shorten the convalescence of these women, and I am fully in agreement with what everybody has said. In order to cure these cases it is necessary to remove the husband and give the patient time to get well. How long it will take is a question. And how can we shorten that time? We know positively that in our cases with mild x-ray dosage, of which we have given the exact technic, these women will be given temporary periods of amenorrhea. As a result of this the inflammatory processes

absorb rapidly and the patients become comfortable, free from pain and are symptomatically cured in a shorter time than with all the methods we have previously used.

I agree furthermore that these cases should not be rayed while they are active. It is after they have been quiescent that we ray them. The point that I am trying to make is that a great many women are operated upon unnecessarily. I hope to have more cases of pregnancy to report in future. So far we have only one out of the 34 cases we have treated. Seven of these cases were operated upon and the rest of them are absolutely well without operation.

**The Kidney of Pregnancy, by DR. JOHN C. HIRST, Philadelphia, Pa.**  
(By invitation.) (For original article, see October issue, page 528.)

#### DISCUSSION

DR. OTTO H. SCHWARZ, St. Louis, Mo.—I was very much interested in one of the last statements the speaker made, that he found no definite relations to the late toxemia and hydronephrosis and pyelitis. This is very definitely our experience in St. Louis. I was somewhat astonished that he felt that the kidney lesion in late toxemia is the primary thing and that the liver is secondary. I do not wish to give the impression that I believe that the liver is the primary condition but it is one phase of eclampsia and the kidney lesion is the other. Whether or not either one of these is the primary factor, I believe we are not able to say until all phases of eclampsia are better understood. The usual kidney lesion seen in late toxemia is very definite and, I think, secondary in origin. Just how the lesion is produced, it is difficult to say.

I feel that there occurs in the kidney a spasm of the arterioles leading to the glomerulus, such as is easily demonstrated in the vessels of the nail bed. It is reasonable to assume that it may occur elsewhere. Thus one might assume that the blood flow through the glomerulus is restricted and the subsequent degeneration of the glomerular cells and cells of the convoluted tubules to be due to inadequate blood supply. Usually this degeneration has reached only the stage of so-called albuminous degeneration, and very little necrosis occurs. Occasionally an arteriolitis of the vas afferens develops. If this does not occur or is not marked, the kidney promptly recovers after delivery.

DR. JOSEPH L. BAER, CHICAGO, ILL.—I experience some paternal pleasure at hearing some one other than myself introduce capillary microscopy into the discussion. It belongs in the type of work that Dr. Hirst has done. I think he will be convinced of its value as a diagnostic aid if he will use it.

Beyond that which Dr. Schwarz has discussed there is the preexisting nephritic damage that persists after pregnancy, the type classified by the essayist as the chronic late gestational toxemia. In these patients the capillaries show permanent and gross distortions which are obviously evidence of prolonged disturbance in the capillary circulation, whereas those patients with an acute toxemia in late gestation show the capillary angiospasm of which Dr. Schwarz spoke.

DR. GUY L. HUNNER, BALTIMORE, Md.—Hofbauer's beautiful work showing the great changes in the entire upper tract, but particularly about the lower end of the ureter, has been most illuminating. There is a great field for work to show just how nature provides for overcoming this physiologic disturbance during pregnancy.

The pregnant woman who develops an acute pyelitis may recover spontaneously in ten days or two weeks just as the nonpregnant does. We are, however, more

particularly interested in those cases that do not clear up spontaneously, the type later seen by the urologist because of chronicity or recurrences. In those cases I have found that the large majority are dependent on chronic narrowing in the ureter. I think that in most instances this narrowing is present before impregnation, and treatment of the narrowing and getting good dilatation enable the patient to go through to term.

A more striking and more interesting type of case is the one that Dr. Hirst mentions, the patient who does not show dilatation but, on the contrary, a lessened capacity in the upper tract, the patient who has had multiple abortions apparently due to kidney failure. I wish to emphasize that there exists in a great proportion of these cases a bilateral ureteral stricture. Do not depend for diagnosis upon whether or not a plain catheter will pass easily. A plain catheter will go through two thirds of all strictures without appreciable obstruction. And do not depend on x-ray plates in these cases. The kidney in most of them, shows a hypoplasia and the pelvis is smaller than normal, the content being only 3 to 5 c.c. perhaps. I have had some of these cases, which, after multiple abortions, have gone through to a full-term pregnancy after bilateral ureteral drainage.

**A Study in Syphilis Based Upon Two Hundred and Fifty Fetal Autopsies, by DR. JAMES R. McCORD, Atlanta, Ga. (By invitation.)**  
(For original article, see October issue, page 597.)

### DISCUSSION

DR. FRED L. ADAIR, MINNEAPOLIS, MINN.—In something over a thousand autopsies we have had only 46 cases of proved syphilis, a percentage of 4.4. Most of these were premature infants. Relatively few fetuses were born alive and only a few born at term.

In the accompanying six graphs the weights of various organs of syphilitic and nonsyphilitic fetuses are plotted against body weight.

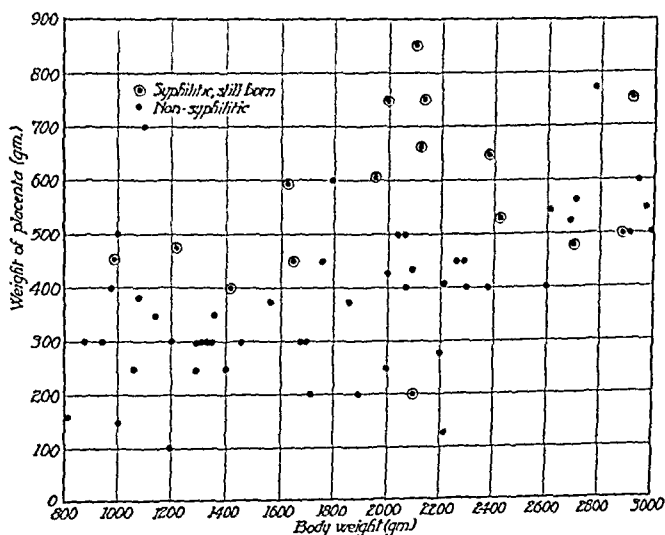


Fig. 1.—Placental weight plotted against body weight. The solid dots indicate nonsyphilitic fetuses, and those with circles indicate the syphilitic fetuses. The placental weight tends to run higher for syphilitic than for nonsyphilitic fetuses.

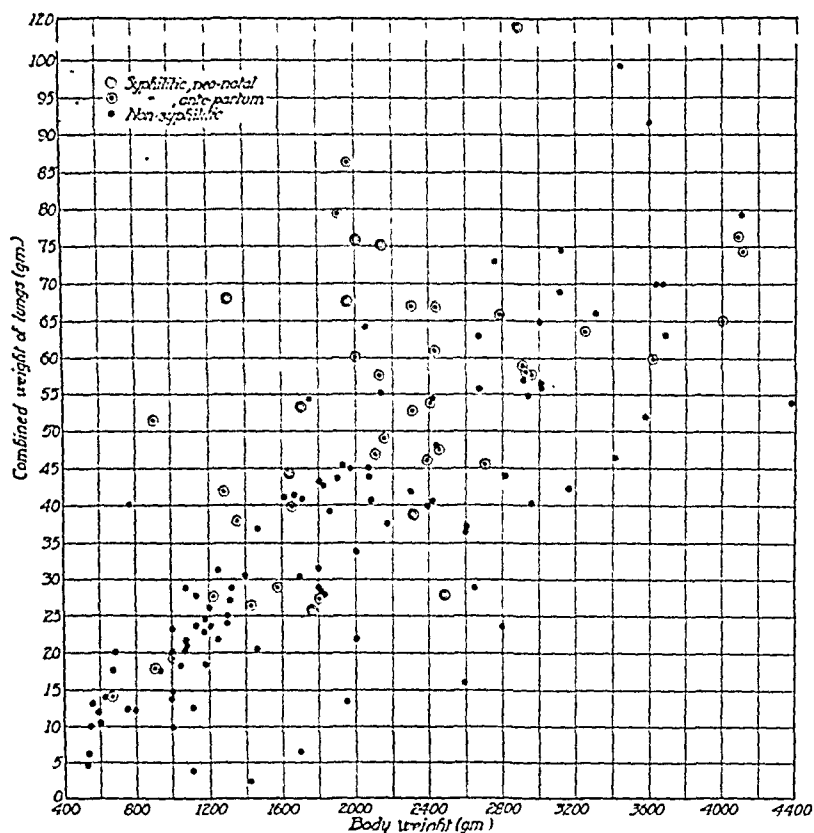


Fig. 2.—Combined lung weight plotted against body weight for syphilitic and non-syphilitic fetuses. There does not seem to be such a marked difference between the lung weight of syphilitic and nonsyphilitic fetuses as compared with body weight. A few isolated cases show an abnormal lung weight for the syphilitic fetuses, and most of these showed evidence of pneumonia alba.

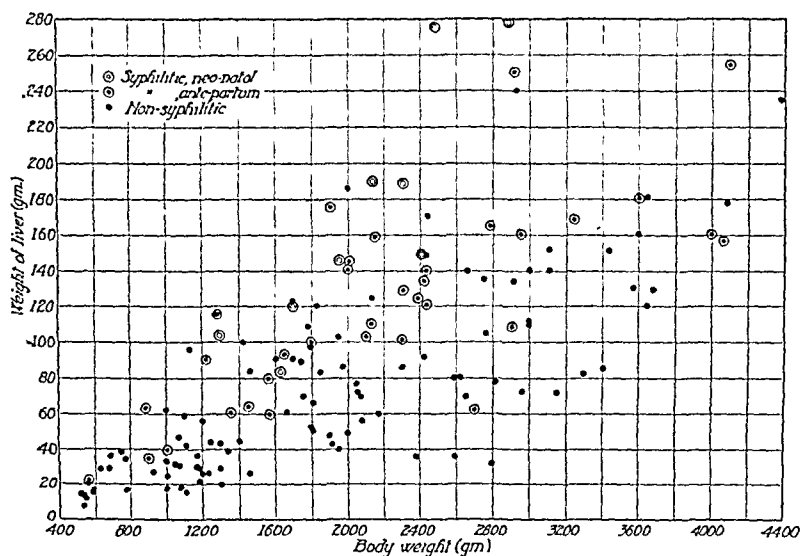


Fig. 3.—Liver weight plotted against body weight indicates a definitely higher organ weight for the syphilitic than for the nonsyphilitic fetuses.



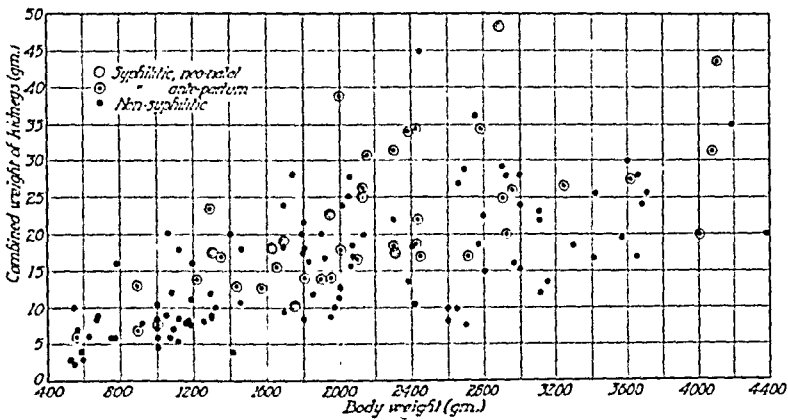


Fig. 4.—Combined kidney weight compared with body weight. There seems to be a definite tendency to a proportionately higher kidney weight in the syphilitic group.

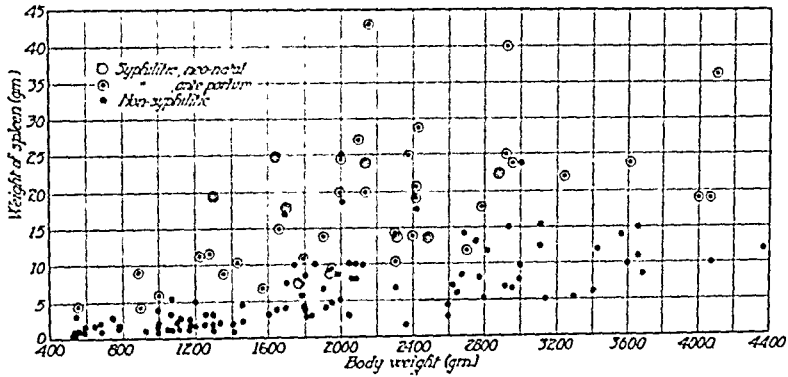


Fig. 5.—Weight of the spleen plotted against body weight shows a definitely higher weight for the spleen in the syphilitic cases.

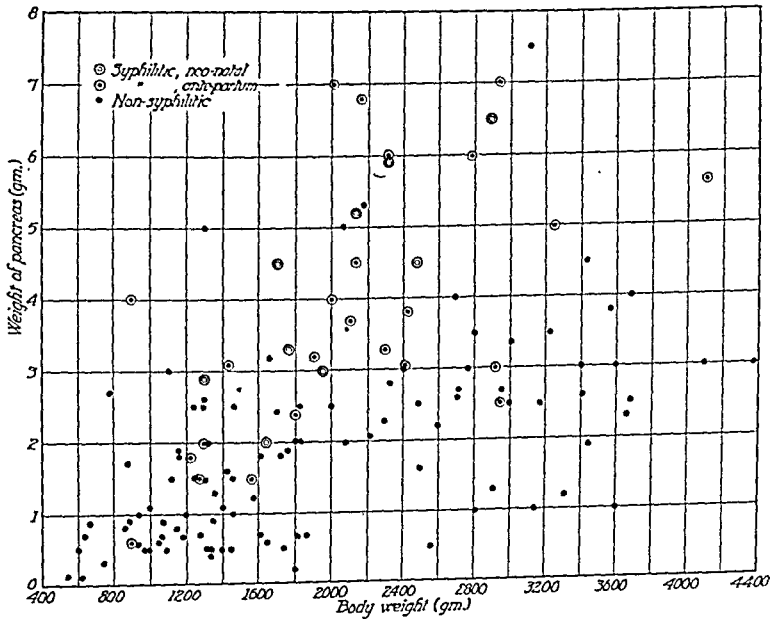


Fig. 6.—Pancreatic weight plotted against body weight shows a slight tendency to a relatively higher weight in the syphilitic fetus.

It is interesting to note that in 31 of 46 cases no clinical diagnosis of syphilis had been made prior to labor. This indicates further need for prenatal care in the attempt to eliminate syphilitic deaths of the fetus.

DR. E. L. KING, NEW ORLEANS, LA.—In the Charity Hospital in New Orleans among the colored patients we have about 18 per cent showing a positive Wassermann reaction, in white patients the percentage is about 2.5. Many of them do not give clinical evidence nor a history of syphilis. We routinely treat all women with positive Wassermans by arsenicals. One patient came to us with a previous history of a stillbirth, and we only had time to give six doses of salvarsan before delivery. The baby was alive and, of course, syphilitic. We believe that routine Wassermann is of great value on account of the high incidence of syphilis in colored patients.

**Leucoplakic Vulvitis and Cancer of the Vulva. Etiology, Treatment and Five-Year Results,** by DR. FREDERICK J. TAUSSIG, St. Louis, Mo.  
(For original article, see October issue, page 472.)

#### DISCUSSION

DR. THOMAS S. CULLEN, BALTIMORE, MD.—Dr. Taussig has covered the subject in a masterly fashion. While he was discussing leucoplakia of the labia, I could not help thinking of the milky patches in the mouth. A certain number of these in due time will develop into cancer. If all of them are operated on promptly, subsequent cancers from such patches are eliminated.

In some cases of leucoplakia of the vulva it is very difficult to cut away all of the diseased tissue without causing considerable distortion. In such instances it is occasionally wiser not to attempt to bring the cut edges of the wound together but to use an ample number of pinch grafts.

While discussing the subject of cancer of the labium, let me mention a patient who had an inoperable chorioepithelioma of the uterus. One of the Bartholin's glands was 2 or 3 cm. in diameter. On making gentle pressure on the enlarged gland, a thin, flat ribbon of tissue emerged from the gland duct. This substance on histologic examination proved to be chorioepitheliomatous tissue, chiefly of the syncytial type.

Block dissection is without doubt the wise procedure in cases of carcinoma of the vulva, and it is preferable, if possible, to do the entire operation at one sitting.

When cutting away the cancerous growth, I have generally employed the cautery knife; and when the growth has been removed, I have cut away the burnt edges of the wound made by the cautery with a knife and approximated the wound edges. In this manner transplantation of cancer cells has been reduced to the minimum.

DR. STEPHEN RUSHMORE, BOSTON, MASS.—There are a few general considerations, suggested or implied by what Dr. Taussig has said, which I want to emphasize. If one looks back into the literature of the subject, the first thing that impresses one is the confusion that has existed, certainly up to recent times. Recent studies have tended to indicate that there is a single underlying process involved in this group of conditions, and the most reasonable view is that we have to deal with a chronic vulvitis, which under certain conditions leads to atrophy, under certain other conditions which are not clear leads to hypertrophy, of which leucoplakia is one manifestation. It is difficult to conceive of a single process that leads to atrophy and at the same time to hypertrophy, side by side. Occasionally we find what we may like to interpret in this way. In acute atrophy of

the liver and some other toxic conditions there is marked degeneration of the parenchyma, even to necrosis. If the patient does not die at once, regeneration of liver tissue begins promptly, often with hypertrophy and sometimes hypertrophy in which cancer has apparently developed. The important clinical fact for us to keep in mind is that in the vulva, if chronic inflammation is associated in its development with hypertrophy manifested in leucoplakia, in a relatively extraordinary number of cases, carcinoma will develop. The way to treat them is, just as soon as we discover that hypertrophic changes are occurring, to remove that area of hypertrophy as extensively as may be necessary in order to prevent carcinoma. This is apparently not true in certain other regions of the body, but leucoplakia hypertrophy of the vulva means carcinoma later in a tremendous number of cases.

What has impressed me most in this study is the remarkable number of recoveries. Carcinoma of the uterus we can cure. Carcinoma of the vulva, a slow-growing process, is very difficult to cure, but with the remarkable number of cures Dr. Taussig has presented I think we all must feel very much more hopeful.

DR. JOSEPH BRETTAUER, NEW YORK, N. Y.—Leucoplakia of the vulva was formerly called kraurosis, after Breisky's publication in 1885. Although this condition is not met with frequently, my records contain at least a score of cases which continued without change for from ten to thirty years; some without any treatment, and others with excision of the entire vulva. None of these cases had the slightest similarity to the pictures shown on the screen by Dr. Taussig. Tumefaction was absent invariably; a purplish discoloration and atrophy of the entire skin from the symphysis down to the rectum were characteristics; none of them developed malignant disease.

The few cases of primary carcinoma of the vulva which came under my observation did not develop on a leucoplakic basis; they proved to be the most virulent type of malignant disease I have met with. None of them lived more than two or two and one-half years, although the inguinal glands were removed as completely as possible.

DR. JOHN O. POLAK, BROOKLYN, N. Y.—Would Dr. Taussig in closing state whether he is still doing this operation in two sittings, as he was doing some years ago?

DR. GEORGE H. NOBLE, ATLANTA, GA.—Radium, though painful, is effective before metastasis has developed but cannot take the place of surgery, for the latter has a wider field of application. It is my opinion that, as a precautionary measure, early removal of the spots is the best procedure.

In removal of leucoplakic spots about the anus, Dr. Taussig states he leaves a bridge of skin to prevent stricture even though all of the diseased area may not be removed. This can be overcome by pulling down the anterior and lateral walls of the rectum until excess of the tissue fills and protrudes beyond the anus. The anterior and side walls of the rectum are loosely attached and several inches of the rectum may be drawn down as I do in complete laceration of perineum and annular stricture of rectum.

DR. EMIL NOVAK, BALTIMORE, MD.—In Dr. Taussig's paper two points stand out as especially important. First of all, it is about as clear a presentation as one could wish of the importance of so-called precancerous lesions. It is natural to draw a comparison with conditions encountered in the cervix uteri. While everyone feels that chronic inflammations and erosions of the cervix predispose to cancer, nevertheless the actual proportion of such lesions which are followed by malignancy is very small.

nant disease must be comparatively small when we consider the very great frequency of the chronic irritative lesions in question. Certainly in the case of the cervix it is nothing like the 50 per cent incidence given by Dr. Taussig for the vulva. It surely is much better to remove these "precancerous" lesions before they become cancerous than to try to cure the cancer after it has developed. Here we have a real field for cancer prophylaxis.

What secondly impressed me were the remarkably good operative results reported. My own experience has been more like that of Dr. Brettauer. How are Dr. Taussig's good results to be explained? One may think that he has been unusually fortunate in encountering chiefly early and favorable cases, though this is not likely. The other explanation which suggests itself is that some feature of the operation he carries out is a real advance on that which most of us perhaps have employed. Many, perhaps most, operators have been content with the excision of the superficial inguinal glands, and it is the excision of the deeper glands, as practiced by Dr. Taussig, which suggests itself as perhaps explaining his unusually good results.

The procedure recommended by Dr. Taussig to prevent postoperative contraction about the vaginal orifice commends itself to me as being well worth while adopting.

DR. CAREY CULBERTSON, CHICAGO, ILL.—The lesions of the vulva are predisposing to carcinoma just the same as the lesions of the cervix. Dr. Taussig has presented this matter before but never with such finality as on this occasion.

One point in regard to the technic. In his previous reports Dr. Taussig has emphasized the importance of doing Basset's operation first and leaving the inguinal wounds to heal, and then doing the vulvectomy. In my own few cases I have followed that procedure and have been criticized for it. The argument is that if one is operating for cancer one should remove all of it at the same time. In my own experience the separate operations have been satisfactory. In one case of carcinoma of the clitoris we did the Basset operation and the vulvectomy, and the patient is doing well. In my last case I had done the Basset procedure on April 23, finding carcinomatous tissue in the left femoral glands, and last week, on May 17, I did a vulvectomy.

DR. WILLIAM P. HEALY, NEW YORK, N. Y.—At the Memorial Hospital in New York City we have been trying to take care of cases of epithelioma of the vulva for about twelve or fourteen years, beginning with the work done by Dr. Janeway and Dr. Bailey, and we have not been so successful in getting five-year end-results with any method that we have pursued, either with radiation therapy alone, surgery alone, or radiation plus surgery. We are convinced that the crux of the matter depends upon two things, the extent of the disease as far as glandular involvement is concerned and the histologic characteristics of the lesion. There is no question whatsoever that some of the largest lesions are the least malignant and can be cured with excision by knife or cautery. The lesions get into the glands not by direct but by embolic extension. A very large lesion may be relatively benign and the glands be not neoplastic but inflammatory. We feel that it is advisable to treat the cases first by radiotherapy, but we cannot treat an extensive case satisfactorily by radiotherapy alone because there is so much local reaction. In a lesion that is extensive, where we are going to do vulvectomy, we plan to follow up the primary irradiation promptly, within ten days or two weeks at the outside, by at least local vulvectomy. In the meantime the glands in the groin are also being irradiated. If they are not neoplastic or of the first or second grade of malignancy, they will respond to radiation satisfactorily; if of grade one or two, they do not respond satisfactorily and will re-

quire removal. We are of the opinion that for a cancer of the fourth grade, the type that Dr. Taussig referred to in the glans clitoris, surgery is absolutely out of place. The only chance such a patient has of being helped is to be placed under radiation therapy because this is the most malignant type of lesion but, as in the cervix, is distinctly radiosensitive and will respond to radiation therapy.

DR. CURTIS F. BURNAM, BALTIMORE, MD.—The divergence of Dr. Taussig's results from those of Dr. Brettauer can easily be understood when you consider the probable type of case each has had.

There are small cancers of the vulva—just as those of the face—which easily can be cured by excision. There are those of low malignancy which either do not metastasize at all or, if they do, metastasize only to the local glands. Such cases will do well with surgical removal.

On the other hand, there are the high-grade malignancies in which the disease rapidly metastasizes after it enters the glands, spreads rapidly through their capsules, and in these cases the operative results are likely to be discouraging.

Leucoplakia occurs in older people, most likely caused by atrophy of the skin. It seems unlikely that the cessation of ovarian function is anything but a concomitant phenomenon. Leucoplakias vary greatly in thickness, in irritation, and in extent. The localized patches are admirably suited to operative removal. In the widespread areas of leucoplakia, monopolar desiccation offers an excellent method of treatment. It also is very effective in the lesions around the anus where operative removal is technically difficult and bad after-results common. In general, leucoplakias are not favorable objects for either radium or x-ray.

In a high-grade epithelioma which is large and fixed and where there are enlarged glands and fixed glands, radiation is undoubtedly the method of choice; and it is possible to cure by this method some of the cases which are not curable in any other way. It would also seem, as Dr. Healy has pointed out, that for the histologic high-grade epithelioma and those cases unassociated with leucoplakia, radiation, even in the operable cases, is preferable to operation.

DR. FREDERICK J. TAUSSIG, St. Louis, Mo. (closing).—While I have had rather striking five-year cures, I am looking forward to the next ten years with some apprehension. My good results may perhaps have been due in part to good luck. As to operative mortality, I have 16 Basset operations without a fatality so far and that speaks very well for its safety. In contrast to the procedure of removing the deep glands through the abdominal route according to Streckel, with a primary mortality of 20 per cent, I think Basset's operation is a safer and more justifiable procedure.

I have been usually following the technic of removing the vulva with the cautery and then trimming the edges with a knife, as suggested by Dr. Cullen some years ago.

In answer to Dr. Polak's question as to doing the operation at two sittings, I am a little disturbed as to how to answer that, for I find myself wavering from one technic to the other. I believe at the present time that if the patient is in good condition for a two-hours' procedure, we had better go ahead and do it all at one time. If she is a poor operative risk, we are safer in doing it in two stages. I believe if the lesion is very extensive and very much infected, it is wiser to remove the vulvar lesion first so as to have a relatively clean field later for the Basset operation, otherwise I would do the Basset first and the vulvectomy later.

Dr. Noble's suggestion regarding the use of the rectal mucosa seems not so applicable in these older women, because if the rectal mucosa pulls away we are

hopelessly lost so far as prevention of a stricture is concerned. I would rather retain the skin bridge on either side to prevent this possible retraction of rectal mucosa.

Dr. Healy's and Dr. Burnam's results with radium and x-ray are, of course, of great value. My own bad results are possibly due to lack of experience. I feel that we should differentiate more than we have in the past not merely as to the malignancy index but as to the point of origin of the carcinoma. Dealing with a glans clitoris or a vestibular carcinoma we should first do a biopsy and in these cases occasionally employ irradiation, but in every case of the epidermal type I think surgery to be preferable.

**Hookworm Disease Complicating Pregnancy, by DR. EDWARD L. KING,**  
New Orleans, La. (For original article, see October issue, page 569.)

DISCUSSION

DR. M. PIERCE RUCKER, RICHMOND, VA.—When you consider how widespread hookworm infection has been in the South, it is evident that any one who has practiced obstetrics in the South must have had many cases associated with pregnancy, but to have recognized it is another matter. The first Rockefeller survey in Virginia showed that in many counties as much as 66 per cent of the population had this disease. A little later, the second survey showed that the incidence of hookworm disease was reduced 2 per cent to 8 per cent. Inquiry of the Health Department and also of doctors practicing in rural Virginia has failed to show any very evident difference in the obstetric results obtained in these counties.

In 1921, at the Spring Street Home, an institution for unmarried mothers, we had a patient with edema and anemia. We found hookworm eggs in the stools, and this led us to make a survey of the population of the institution. We found 25 per cent infected with hookworm. I thought this possibly might have been a factor in their delinquency. We found these girls coming from rural Virginia. Later we had a city crowd and the hookworm infection disappeared. None of these cases was severe. The lowest hemoglobin was 65 per cent, and there were no obstetric complications. All of them went to term and had live babies. Looking up their histories later, I found that all these patients in the puerperium complained of headache and most of them had red lochia for several weeks. That seemed to be the only clinical difference between this group and the other cases.

In regard to treatment, I am glad to hear Dr. King say that it is safe to treat them during pregnancy. I did not treat any of them until after they were confined for fear of producing abortion. I do not think that the mild infection plays any rôle in obstetrics.

DR. B. P. WATSON, NEW YORK, N. Y.—I had my first experience with hookworm disease just two weeks ago in New York City. The patient had been delivered in the Sloane Hospital two years ago by cesarean section. At that time she had been very anemic with only two million red cells and 40 per cent hemoglobin. When she returned to the clinic in her second pregnancy she was still anemic. We are making a special study of the anemias of pregnancy, and in the course of the routine stool examination the hookworm eggs were discovered. The patient came from the West Indies but has lived in New York during the last six years. The patient is now seven months' pregnant and requires another cesarean. We have been afraid to carry out any treatment for the hookworm disease for fear of dire results. I am glad to have the assurance that treatment can be carried out safely during pregnancy.

DR. E. L. KING (closing).—At first we hesitated to treat these patients. We had one or two instances where the patient aborted or delivered prematurely and lost the baby, but this was not due to treatment. Since we have adopted the procedure of treating them as soon as they are admitted, sometimes several times before delivery, our results have been better. Our system is to treat them every eight or ten days. It takes about that long for the thymol to disappear, and thus we avoid the possibility of thymol poisoning. Since doing that we have had no trouble from abortion or miscarriage. Lambert said he had treated several hundred cases without abortion. Isfram had followed 60 cases, with several abortions, but he felt that the treatment was not responsible. The same experience is reported by Soper.

We had taken it for granted that hookworm disease had been eradicated, and then in New Orleans picked up about 30 cases in a ward that was not a medical ward. The patients came in solely for the pregnancy. It does appear that there is an increased frequency of toxemias in these very ill women.

**Trichomonas Vaginalis, Donné, by DR. CARL H. DAVIS, Milwaukee, Wis.** (For original article, see October issue, page 575.)

#### DISCUSSION

DR. CAREY CULBERTSON, CHICAGO, ILL.—Some clinicians find trichomonas frequently in cases of chronic vulvovaginitis; others find it very rarely. I am one of the latter group and thus not the proper person to discuss Dr. Davis' paper with the idea of adding anything new to his very elaborate studies.

There is still some doubt as to what trichomonas is, whether it is pathogenic or not, whether it is identical with the similar organism obtained from the intestinal tract. Parasitologists are not helping us, for they seem to think that it is not a pathogenic organism, but an organism found nonpathogenic in the laboratory may be pathogenic in man. Certainly the work done by Dr. Davis and others would seem to be very conclusive that a chronic vaginitis is due to this organism. This seems to be more common in our private patients of childbearing years, in the multipara, and is not often seen in the nullipara or single patient. We do not seem able to discover the *Trichomonas vaginalis* in the patients who come to the dispensary. At the Cooke County Hospital the same thing is true. Why this should be so is not clear.

DR. FREDERICK C. HOLDEN, NEW YORK CITY.—During the last four months we have isolated this organism by the hanging drop in our office in 19 cases. We have found them in virgins, during pregnancy, and postmenopausal. In one case they were found while a Huhner test was being made. It is interesting to note the variations of symptoms, some women complaining of very little leucorrhea and vaginitis, some being treated for gonorrhea over a long period of time with a great deal of discharge, severe irritation and burning. These cases may be easily mistaken for g.c., as the clinical picture is identical in some cases. Some of these women have been operated on, and others have been in the hands of many doctors for a period of years without relief. To date, we have only one cure, as we do not consider the case cured until we have had negative hanging drops after at least three to four successive menstrual periods, all treatments having been discontinued during this time, not even simple douching being allowed. Most of our cases have not yet had time to fulfill this condition. It is a relatively simple matter to rid the patient of organism and symptoms with a few treatments, but following a menstrual period they usually return with many organisms pres-

ent. For this reason we are now having these patients treat themselves during the menstrual period. They instill 4 c.c. of mercurochrome with an aseptol syringe night and morning, and we hope in that way to shorten the treatment.

DR. HUGO EHRENFEST, St. Louis, Mo.—Dr. Davis mentioned the fact that there is some doubt as to whether there exists a real *Trichomonas vaginalis*. Personally I have been convinced for a long while that there is a specific trichomonas vaginitis for the simple reason that I feel I can almost make the diagnosis when examining the patient. The discharge is peculiarly characteristic. It has a pale yellowish-greenish color and is thin. Furthermore, when it contains little bubbles, one will invariably find the trichomonas.

In regard to examination, Dr. Holden advised the hanging drop. I think that this is an unnecessarily complicated procedure. If you simply put a drop under a cover glass, using a little pressure, you see big fields of leucocytes, and within them small lake-like areas, open spaces probably filled with serum, and along the edges of these clear areas you will readily see the wriggling trichomonas. In this manner the microscopic diagnosis takes only a fraction of the time required for a hanging drop or a smeared stain. There is no doubt that trichomonas are very often found.

My results with treatment are not very satisfactory. Just two or three days ago I saw my first case of typical *Trichomonas vaginalis* in a virgin. I have seen the condition often in pregnant women and I may mention that statistics have been published which tend to establish a relation of the *Trichomonas vaginalis* to puerperal morbidity.

DR. IRVING F. STEIN, CHICAGO, ILL. (guest).—It will require a great deal more work before we have a satisfactory form of treatment. I agree with Dr. Davis that the trichomonas is probably pathogenic. I have looked upon it heretofore as an incidental invader or possibly a symbiotic organism, until I began to concentrate upon the picture, and, as Dr. Ehrenfest has said, the picture is so lucid in a chronic case that immediately the patient tells her story one may suspect that she has a *Trichomonas vaginalis*.

I recently had a patient, a 23-year-old girl, who said that she was willing to have an hysterectomy in order to cure her leucorrhea. Her family doctor had cauterized the cervix three times and had given treatment for a year, had performed a plastic operation on the vagina, but the condition was not improved. The history was absolutely typical of this condition. On inspection we found the picture of diffuse mottling, reddening in the introitus. On separating the labia a stream of milky yellow discharge appeared containing bubbles, which on the hanging drop examination yielded numerous trichomonas. The point about the hanging drop is that if you take the plain drop the pus cells are so numerous that one often finds difficulty in locating the trichomonas, but if it is diluted with physiologic saline solution, they are more easily seen and appear to be much more active. While introducing a speculum the rugae are intensified, and there are often little bleeding points. In the cervix instead of finding the mucopus of a gonococcal endocervicitis one finds a clean endocervix but strawberry-like red spots on the portio that are very characteristic.

The trichomonas found in the vagina may be an offspring of the intestinal type. There are four types described, one type, as you know, is found in the mouth, one in the lung, one in the bowels, and one in the vagina. Dr. Davis was unable by culture to grow the vaginal type on the media used successfully by Heguer for the intestinal trichomonas. Perhaps that is due to their being in a new environment, and perhaps it is a different strain of trichomonas.



DR. JOSEPH P. DELEE, CHICAGO, ILL.—I have had nine or ten years experience studying trichomonas. There are several varieties. Under the microscope you can see two main varieties, one with a little tuft of rapidly moving cilia at the end, and another with a long single cilium that waves quietly to and fro. These latter are the most difficult to cure. Some of the obstinate cases have recovered when I have treated them generally as well as locally. I found by giving them iodine or thyroid, depending upon the basal metabolism, that the local treatment is more successful. So I believe there are certain conditions of the general system that so affect the vagina and its secretions that the soil in which the trichomonas grow is more or less fertile and in treating the general system I have aided the cure. That does not mean that one should neglect the local treatment, and I have found the old remedy recommended by Hochne is the best, soda and glycerine.

In addition to that, you must cure if possible any associated endocervicitis, so the cautery has its place in those cases that are complicated with trichomonas. I want to mention its relation to puerperal morbidity. It does increase morbidity, and during pregnancy up to six weeks before delivery it is advisable to try to treat the discharge.

In our dispensary service we find it as frequently as in private practice, and in primiparae as much as in multiparae. Very recently a world famous surgeon did a hysterectomy to cure a simple case of this kind. The woman had been driven nearly insane by the irritating discharge and the fear of cancer. At first a doctor took out her tubes and ovaries, a second doctor did a hysterectomy which did not cure the discharge, and a third surgeon removed a granuloma which developed in the vagina and that did not cure it. One of my assistants made the woman comfortable after the third treatment for trichomonas.

DR. OTTO SCHWARZ, St. LOUIS, Mo.—In the cases where the symptoms are unusually frequent and where the organisms are unusually prevalent, what happens to the ordinary bacterial flora of the vagina?

DR. JOSEPH L. BAER, CHICAGO, ILL.—I do want to make just a few points: first, the extreme ease with which the flagellates may be found in the hanging drop with dilution, this being decidedly preferable to the slide in our experience. Second, the frequency with which they are found. There is no question that if we search for them we will find them in a vast number of patients. We have not found trichomonas in women past the menopause, possibly because they thrive best in blood media. In patients under treatment they flourish best just after the menses. No published microscopic study has shown the presence of this parasite buried in the tissue, nor have any actual tissue changes been described which could be ascribable to the invasive pathogenicity of the trichomonas. This has a possible bearing on the conclusion of most of the European clinicians that the trichomonas is harmless and symbiotic. Most of our patients had a preexisting gonorrhea, the trichomonas being found subsequently, both in the presence and in the absence of the gonococcus.

We have thus far failed to convince ourselves that we are really eradicating the trichomonas from the patients whom we treat. We have tried the green soap scrubbing, mercurochrome, lactic acid, sulpharsphenamine and chlorazene dissolved in water and incorporated with glycerine, yet essentially the relief that is immediate can be obtained with a simple glycerine tampon. But the condition tends to recur. At present we are limiting our follow-up treatment to painting with 10 per cent silver nitrate.

DR. N. P. SEARS, SYRACUSE, N. Y.—I have had about fifty cases but cannot give detailed statistics as to the number of unmarried and married women. I find the condition very frequently in virgins and am inclined to believe that the infection comes from rectal contamination. I had one case, a multipara, who had a small rectovaginal fistula, and I have been unable to stop the discharge. The treatment I have used is an old one, a thorough painting with tincture of iodine and a 4 per cent to 5 per cent lactic acid douche. The iodine is used every fourth day and the other treatment given in between. When I first encountered this organism, I tried everything in the vain hope of curing the vaginitis.

DR. E. D. PLASS, IOWA CITY, IA.—I would like to add one observation which may complicate the etiologic aspects of this disease. We have found not infrequently that the infection is complicated by a monilia infection. French writers have described a yeast vaginitis, and in a few instances we have been able by the use of an acid culture medium to grow the yeast. This introduces the problem as to whether the yeast has any etiologic significance. We have attempted to run controls and have found that the vaginal secretion usually does not harbor yeast. Whether there is a symbiosis between the two types of organisms, we are as yet unable to say, but I thought the observation should be reported.

DR. CARL H. DAVIS (closing).—In only one case have I found trichomonas associated with yeast. During the last few months I have had a number of cases of very severe yeast vaginitis and most of these women were past the menopause; only one was menstruating.

In the 50 cases of trichomonas which I have had, it was not possible to demonstrate the gonococcus in a single instance.

I stopped the routine use of silver nitrate and of iodine because a number of patients have developed severe burns which took a long time to heal. Drugs should be used which will only kill the trichomonas without further injury to the already inflamed mucous membrane.

Regarding the changes in the vaginal wall, one finds that after the pus cells begin to disappear there is a tremendous desquamation, and a patient is not considered cured until she has a normal vaginal secretion. If treatment is stopped too soon, the patient will within a few weeks return with a very severe trichomonas vaginitis, and this leads me to believe that perhaps some of the parasites are harbored in the inflamed mucous membrane.

I have had several patients past the menopause with a trichomonas vaginitis.

Patients who do not have coitus, if they are treated sufficiently, eventually show a perfectly normal vaginal bacterial flora.

The symptoms which Dr. Ehrenfest mentioned are perfectly typical of the patient who comes without previous douching or other treatment. If you get a patient with a history of a persistent vaginal discharge insist that she go for at least forty-eight hours without a douche and then you will be in a position to tell whether or not she has trichomonas.

I cannot agree with Dr. Culbertson that this condition is more common in private practice than in dispensary practice. At the Milwaukee County Dispensary it was found that of the women who came in complaining of discharges approximately 33 per cent had trichomonas.

I purposely did not make any statement regarding cures because, while I have a number of patients who have remained cured for more than a year, I am still wondering whether or not there is going to be a recurrence. After another two or three years I will be willing to talk about cures. I cannot agree with Dr. Baer that it is not possible to cure these patients. The treatment used by Dr. DeLee was outlined in our first paper.

**Auto Blood Transfusion in Gynecology**, by DR. LILIAN K. P. FARRAR, New York, N. Y. (For original article, see *Surgery, Gynecology and Obstetrics*, October, 1929.)

**A Review of Breech Deliveries Over a Five-Year Period**, by DR. WILLIAM C. CALDWELL AND DR. W. E. STUDDIFORD, New York, N. Y. (For original article, see page 623.)

#### DISCUSSION

DR. E. B. PIPER, PHILADELPHIA, PA.—In Minneapolis last year, in the obstetrical section, we presented a paper on the routine use of after-coming head forceps, in all difficult breech extractions, to decrease the fetal mortality and also the morbidity. A neurologist followed that paper with a large number of photographs showing the horrible results of breech extractions from the neurologic standpoint. Now we believe and state that this is due, as Dr. Caldwell said, to injury of the tentorium, broken necks, injury to the brachial plexus and injury to the nerves of the cervical plexus, and that these injuries may be avoided by the routine use of forceps.

My own statistics cannot well be compared with those of Dr. Caldwell because I understand all of his were natural breeches, none being produced by version. However, in the Philadelphia Lying-in Service there were nineteen breech extractions with a mortality of three, a percentage of 15, which looks bad. The three deaths were due to premature twins and one twin macerated, and the third was a craniotomy. So cutting those three out we have no deaths due to delivery itself. All were delivered by means of the after-coming head forceps. In the University Hospital we had 38 cases and 7 deaths, a percentage of 18.8. Four of them were premature infants of seven months or more; two were placenta previa; and one had a diabetic mother in whom the fetal heart sounds had not been heard. That explains these seven deaths. Therefore, we had these two series of 19 and 38 breech deliveries without a fetal death due to delivery itself.

I am inclined to think that in doubtful cases of breech delivery, the elective cesarean would reduce the mortality better than any method of delivery.

I do not agree with Dr. Potter's assertion that you can always do an extraction with the anterior arm first. In a recent case I took the posterior arm on one side, started to do it on the other side and could not without fracturing the whole shoulder. I then put on the forceps and got the arm out with the head without a fracture of the arm. One can do many things with the forceps. It is entirely immaterial, I think, what forceps are used, in some cases the old Tarnier forceps, in some the Dewees', depending on what the operator is accustomed to. Personally I like the ones I have designed for myself.

DR. H. C. BURGESS, MONTREAL, CANADA.—Practically all available records show, and most authorities agree, that the infantile mortality in cases of breech delivery exceeds that of vertex presentation, and any contribution that tends toward a solution of this problem deserves to be commended.

In 1924, I reviewed over 18,000 cases occurring in the Montreal Maternity Hospital, and demonstrated that in contracted pelvis, the operation of version and extraction showed a higher infantile mortality than any other method of delivery, except craniotomy; and in a review of the 9,000 cases occurring since that date three important facts stand out very prominently: first, that the operation of version and extraction in this class of case has been performed much less frequently; second, that where attempted, the infantile mortality has been greater than in the previous series of cases; third, that elective cesarean section has been the operation of choice.

As far as I am concerned, the solution of this problem has been reached. Given a breech presentation, I attempt from the thirty-fourth week onward to perform an external version; and where I have been successful in this manipulation, no contrivance has been necessary to keep the fetus in its new position. If I fail in this manipulation, or if there is a history of dystocia in previous labors, or if the diagonal conjugate measures 11 cm. or less, I advise a continuation of this pregnancy and delivery by cesarean section at or near term.

The obstetrical staff of McGill University has decided against teaching of this external version to students, fearing that the inexperienced practitioner may be mistaken in the diagnosis or fail in his manipulation and transform a longitudinal presentation into a transverse. We urge him in this class of patient to study the pelvis, and if he finds any degree of pelvic contraction, to induce labor from the thirty-sixth week onward, and to leave the laboring patient alone until the breech is born through the vulva. For the induction of labor the bougie proves more efficacious than the bag.

DR. HUGO EHRENFEST, St. Louis, Mo.—The importance of external version as a prophylactic measure has been mentioned. Reference was made to the paper by Bartholomew, and at the time when it was presented I cited my own results with external version. I have practiced it routinely for probably fifteen or twenty years. In every discussion of the problem of breech labor and external version some one seems to assert that we do not need prophylactic external version because we can make breech delivery practically free of danger. It is obvious that no fair comparison can be made of statistics on external version submitted by one man with statistics of another man concerning his own results in breech delivery. So I thought I would study the results of both procedures on my own cases. I have analyzed a consecutive series of 518 private cases, all having received proper prenatal care. I found I had made 11 successful external versions in recognized breech presentations with loss of one baby, and in the same series had 11 breech labors with three fetal deaths. The one baby lost after successful external version, as a matter of fact, was sacrificed in an inevitable craniotomy, so that it cannot be counted against external version. Among the three babies lost after breech labor there was one case of enormous cystic degeneration of the kidneys, and that case again should not be counted against breech labor.

That leaves in the entire series only two fetal deaths occurring in breech labors, and the analysis of these two cases proves very instructive. The one was an elderly primipara with a typical, long labor. Baby was fresh dead. With all my experience in version I cannot help feeling that the baby certainly would have had a much better chance if the diagnosis could have been made and a version performed at the proper time. The second case was a woman with a slightly funnel-shaped pelvis. She had in her second pregnancy a breech presentation which was recognized. External version was done and the baby delivered alive. In the third pregnancy I had overlooked the breech presentation and this baby was lost. Personally I am forced to the conclusion that if I had recognized in both these cases the existing breech presentation and done a version, in the one case the baby would have had a decidedly better chance to survive in a vertex labor, and in the other case, with the satisfactory result in the preceding labor, with proper diagnosis and version also this baby would have been saved. So I feel that this series of 518 consecutive labors proves beyond doubt that external version has its very definite advantages and greatly reduces the fetal mortality incident to breech labor.

DR. HARVEY B. MATTHEWS, BROOKLYN, N. Y.—I can subscribe to the conservative method of breech delivery that Dr. Caldwell has outlined in toto. I believe that full dilatation of the cervix coupled with plenty of time in delivery is

most important. I believe most of the babies that are lost are lost on account of too much hurry in delivering the breech and after-coming head. At the Methodist Episcopal Hospital, during the past two and a half years, there were 192 breech presentations and 22 versions, making a total of 214 breech deliveries. The percentage of stillbirths was 12.1 per cent. At the Long Island College Hospital during the past year there were 44 breeches with an incidence of 15.2 per cent stillbirths. These figures include all viable babies.

DR. JOHN O. POLAK, BROOKLYN, N. Y.—There is one teaching that we give and try to disseminate: after the cervix is fully dilated and the breech has presented and is out of the vulva, we teach "Do not pull. Let her push and you guide." We try to make that so impressive that our students and our interns will follow it throughout life. The result has been that we do not look upon the breech case as the formidable case we previously did.

I feel, furthermore, in regard to external version that it would have become a head presentation if it had been left alone, or there is a condition responsible for the breech presentation that even external version does not remove. In the cases of minor degree contracted pelvis the elective cesarean section is a life saving procedure in breech delivery.

DR. JOSEPH P. DELEE, CHICAGO, ILL.—Everybody knows and agrees and is willing to admit that injury kills a lot of babies during breech delivery and that hemorrhages into the brain and all the other things mentioned are very common. I wish, however, to make a little qualification that delivery itself does not injure quite all of the babies. I think Dr. Burgess hit the nail on the head in every respect but one. I would qualify his condition for cesarean section. I think that with a large baby and narrow pelvis a cesarean section is the proper thing, but to make the indication quite as broad as he did seems wrong to me. A little test of labor in these breech cases will help a great deal, and therefore I let these women go into labor when I have good reason to believe they will come through all right, and I believe this is the proper thing to teach.

By means of a stereoscopic x-ray study one gets a better idea of the size of the head and its relation to the pelvis than with the simple x-ray. It will also reveal a monster, and the frequency of monsters in breech presentation is remarkable. At the Chicago Lying-in Hospital in 1926 and 1927, 6,031 births in the hospital had an incidence of 250 breeches, 4.1 per cent. The reason for this high percentage is that we have a large number of referred cases of breech delivery. Of these 250 breech cases, breech extraction was performed 166 times, cesarean section 43 times. In the remaining 41 cases the labor was spontaneous or manual aid was necessary. In the 250 cases (103 primiparas, 147 multiparas) there were 24 fetal deaths, 14 babies were stillborn and 10 died later. Deducting from these 24 babies, those dead on admission, monstrosities, syphilitics, intestinal obstruction and the eclamptics, we have a corrected mortality of 14 deaths in 250 breech cases, or 5.6 per cent.

Some of this mortality could be further reduced if we had had autopsies on all of the babies. Omitting the babies that were delivered by cesarean section, we have a fetal mortality of about 6 per cent. Now does that 6 per cent mortality justify cesarean section with a mortality of 1 to 16 per cent of the mothers? Should we not restrict, certainly in our teaching, this operation if with ordinary care the case can be so safely cared for? Would an infant mortality of 6 per cent or even of 10 per cent justify the increase in the already widespread use of cesarean section in breech cases?

DR. E. L. KING, NEW ORLEANS LA.—About a year ago Dr. Gladden and myself reported a series of 159 breech deliveries. We eliminated all premature babies and all babies dead before delivery was attempted; in other words, taking only healthy babies at or near term. We found a mortality of a little more than 10 per cent, 16 babies out of 159. The fetal mortality was higher in multiparas (12 per cent) than in primiparas (6 to 7 per cent). I think that is due to two causes: first, the babies of multiparas were larger—on the average over a pound—than the babies of the primiparas; second, there is a tendency to underrate the seriousness of breech delivery in a multipara.

I feel that external version is a wise practice.

Another factor which influences the fetal mortality is the time of intervention. My teaching is that the case should be left to nature and that assistance should be given only when it is necessary. In hospital work, however, where we have every facility, in most cases I deliver the baby under deep anesthesia as soon as the cervix is fully dilated, especially in a primipara. I believe in that way we have lowered the fetal mortality.

I agree with Dr. Piper that the forceps on the after-coming head is a measure of considerable value. Certainly it has helped me in a good many difficult cases. I also feel that cesarean section is a procedure to be reserved for patients with narrow pelvis, or for elderly primiparas.

DR. WILLIAM C. CALDWELL (closing).—I agree with Dr. Piper that forceps on the after-coming head are frequently useful. Doctors Irving and Goethals were able to reduce the infant mortality in breech presentations over one-third by concentrating the breech deliveries in their own hands.

The mortality in breech presentations will be greatly reduced by not interfering with a normal advancing labor, by thoroughly preparing the birth canal before starting a breech extraction and by taking plenty of time in the delivery even though the baby should inhale some amniotic fluid. Even slight angulation or forced traction is likely to result in serious injuries to the child.

**Cancer of the Uterus Complicating Pregnancy**, by DR. JOHN A. MCGLINN, Philadelphia, Pa. (For original article, see October issue, page 592.)

#### DISCUSSION

DR. WILLIAM P. HEALY, NEW YORK CITY.—We feel like Dr. McGlinn that the cancer is the important problem to be considered and that its treatment should be that which we in our individual experience regard as the best suited to the cure or treatment of the existing cancer regardless of the complicating pregnancy. We use at the Memorial Hospital a very massive radium dosage, applied per vagina, and heavy x-ray therapy. With radium applied within the cervical and uterine canals, we expect the fetus to die, certainly that it will not go to term, therefore we ignore its presence.

The question of early diagnosis is the important one; I would like to emphasize the care with which biopsies in these cases should be done before resorting to any therapeutic procedure.

I am inclined to believe we may have a higher incidence of carcinoma in primiparas in the future as the result of the prevailing birth control tendency and late marriages. We now find more women entering the cancer age though still awaiting their first child. Therefore, we shall probably see more cervical cancers in primigravidas.

We are very definitely against hysterectomy in the treatment of carcinoma of the cervix that has developed during pregnancy and prefer to control the lesion with high voltage x-ray and radium.

DR. JAMES C. MASSON, ROCHESTER, MINN.—We saw three cases of pregnancy complicated by epithelioma of the cervix. One patient was about seven months pregnant with an extensive inoperable growth. We allowed her to go another month and then did a Porro-cesarean, obtaining a living child. The malignant growth was treated with radium afterward, but the mother died four weeks after the operation as the result of a pulmonary embolus.

The problem was different in the other two cases. They were both four months pregnant and had very early malignant lesions. I operated both of them. The microscopic evidence of the tissue is very important, and the degree of malignancy found (Broder's classification) should influence us a great deal in deciding whether a case should be treated surgically or by radium or x-ray. Even a small growth of a high degree of malignancy is better treated by radium in most cases. On the other hand, if a small growth is of a low degree of malignancy, the prospect for cure by surgery is very good or, probably better, by surgery plus radium and x-ray. Both of these cases were early lesions and of grade 3 according to Broder's classification. In these two cases I made a combined vaginal and abdominal hysterectomy, first separating a cuff from the vault of the vagina and then going in from above and doing a wide dissection in the base of the ligaments, hoping to avoid cutting into malignant tissue. Both operations were done about eighteen months ago and I saw one of the patients a month ago and have heard from the other regularly every three months. They are both in good condition.

I think one important consideration when pregnancy is complicated by epithelioma of the cervix is the danger of sepsis if the uterus is emptied but not removed.

DR. ARTHUR H. CURTIS, CHICAGO, ILL.—My experience has also been limited to three cases, one 28 years old who about twelve years ago was treated with radium, another two or three years later about 32 years of age, and a patient whom I saw with Dr. DeLee several years ago, about 35 years of age.

I wish to emphasize that cancer of the cervix in a patient who is pregnant is more difficult to diagnose than the ordinary case of carcinoma. The lesion tends to be very much magnified by the pregnancy, just as fibroid tumors often grow much larger during pregnancy. If I ever encounter more patients with extensive carcinoma of the cervix complicating pregnancy, I shall do all possible in therapy even though the outlook appears to be hopeless.

DR. CHARLES A. BEHNEY, PHILADELPHIA, PA. (guest).—About thirteen years ago a patient was seen by Dr. Keene. She was 26 years old and had seven or eight months before been delivered of a normal child. She had a squamous cell carcinoma of the cervix and was about six months pregnant. Dr. Keene did a cauterization of the cervix and applied 100 mg. of radium for 36 hours. When seen about two months later the cervix was partly dilated and labor apparently about to begin. She was delivered of an apparently normal child without any great difficulty. Before she was discharged, Dr. Hirst applied 100 mgs. of radium for 36 hours more. The patient is well today, but the child developed into a microcephalic idiot.

DR. WILLIAM P. GRAVES, BOSTON, MASS.—I wish to say a few words concerning the influence of radium on the fetus when it has been applied previous to conception. We have in our series 30 cases where nonsterilizing doses of radium had been given for uterine insufficiency in women capable of later child-bearing.

In following up these cases we found that 13 women had conceived later, there being a total of 20 pregnancies. From these pregnancies there are 8 living children. The remainder of the conceptions ended in abortion or premature birth or in very early death after birth. An attempt was made to determine the physical character of the living children, the data being based for the most part on letters from the mothers. In all cases the mothers reported that there were no deformities, excepting one in which there was said to be some malformation of the nose. From the large percentage of miscarriages it might be inferred that the radium had had some deleterious influence on the endometrium. On the other hand, it must be remembered that all of these patients had been treated for abnormal bleeding and that the tendency to miscarriage may have been constitutional rather than from the effect of irradiation.

DR. FLOYD E. KEENE, PHILADELPHIA, PA.—I will add one other new case. This patient was between three and one-half and four months pregnant, and the cervix extensively involved by a malignant growth. I did a supravaginal hysterectomy and bilateral salpingo-oophorectomy as a primary procedure. Two weeks later, I did a wide cauterization of the cervix and applied 2400 mgh: of radium element. This operation was performed about two years ago, and at the present time the patient is in perfect health with no evidence of malignancy.

I should like to second Dr. Graves' statement regarding preconception irradiation. Dr. Murphy's very careful investigation of this subject, as well as our own experience in following up patients who have become pregnant after irradiation, convinces me that there is little or no danger of deformities or anomalies developing in children born after radium has been used. On the other hand, I am equally firmly convinced that not infrequently very serious abnormalities may follow upon postconceptional irradiation.

DR. G. B. MILLER, WASHINGTON, D. C.—In Veit's handbook can be found a very comprehensive article on carcinoma of the uterus in pregnancy. I think it pays to read it.

I have had only one case, a woman who came to the Columbia Hospital in the eighth month with a cervical cancer which was regarded as incurable: therefore, the doctor who saw her discharged her with instructions to return when in labor. When I saw her I felt more hopeful in regard to cure. She was at term and in labor. I did a cesarean and followed it immediately by a radical Wertheim operation. The edema of the tissues in the pelvis made the separation of the ureters and tissues around the cervix extremely easy. That was done 16 years ago, and the patient three years ago was still alive and well.

DR. JOHN A. McGLINN (closing).—With the increasing use of irradiation in stimulating doses for various functional disorders and for adolescent bleeding in women, this subject assumes great importance. We have fairly definite knowledge of the effect of irradiation on the fetus during pregnancy. We are not so sure of the effect on the fetus of preconception radiation. This is one of the most important subjects in our specialty to be worked out at the present time.

**The Significance of Low Arterial Pressure in Pregnancy**, by DR. PHILIP F. WILLIAMS, Philadelphia, Pa. (By invitation.) (For original article, see October issue, page 546.)

#### DISCUSSION

DR. BARTON COOKE HIRST, PHILADELPHIA, PA.—Like most practitioners I have two or three of these cases constantly under supervision, and a puzzling minor complication of gestation it is. I have an advantage over Dr. Williams which he



need not envy. I am seeing my second generation of patients and have under my charge now a young woman who presents this peculiarity in a marked degree. I had charge of her mother when this girl was born, and I believe that her hypotension and general nervous instability had its origin in her intrauterine existence. Her mother had grave domestic difficulties during her pregnancy and this probably accounts for her daughter's low vitality.

Another case can be attributed to the same cause, but the father was at fault. He was in a state of extreme nervous instability and tension when his daughter was procreated. This daughter during her pregnancy not only had a low blood pressure but a curious lack of initiative. Her attendant had to get her out of bed in the morning, make her put her stockings on, brush her teeth and so on, or she would have done nothing on her own responsibility.

My experience differs a little from Dr. Williams' in regard to treatment. If the systolic blood pressure is as low as 80, these patients are put to bed for several days and are given powdered digitalis and strychnia. Almost invariably their blood pressure rises in response to this treatment.

Dr. Williams did not emphasize the fact, if I heard him correctly, that there is a persistent tendency in all pregnant women to a low blood pressure. The majority of pregnant women have a blood pressure under normal. If it is much exaggerated, an explanation may be found in the girl's intrauterine existence. These patients are almost always lacking in nervous vigor and often show more or less imperfect physical development. Under observation and treatment, with periods of complete rest, they can be guided through their pregnancy successfully and need not experience any special difficulty in their parturition and recovery, although it is my routine practice to give them a course of cardiac stimulation for a short time prior to their expected delivery.

DR. HERMAN J. BOLDT, NEW YORK, N. Y.—Is not the low blood pressure mentioned by Dr. Hirst due to a nervous condition rather than to the pregnancy? It is a matter of fact that almost every person who is exceedingly nervous and highly neurotic will have a blood pressure below normal.

DR. BARTON COOKE HIRST, PHILADELPHIA, PA.—The persistent low blood pressure in all pregnant women cannot always have a nervous origin. There is probably something in pregnancy which accounts for it because at other times these patients may be perfectly normal in this respect. The explanation may be found in a lack of muscular development in the left ventricle to keep pace with the added volume of blood that it must propel through the body. In the exaggerated cases under discussion there is, I think, the added factor of impaired nervous vigor.

DR. ARTHUR H. MORSE, NEW HAVEN, CONN.—My personal experience with hypotension has been in those patients who have gone through a prolonged labor, or upon whom an operative procedure has been performed. We have had patients in the wards, and I have personally cared for a number of private patients in whom the systolic pressure was low, though not as low as in the cases which Dr. Williams has reported. I have never been particularly concerned about those patients. Generally the pressure has risen toward the end of pregnancy, and the patient has gone through labor, as far as I have been able to determine, quite as satisfactorily as those in whom the pressure was higher.

DR. OTTO H. SCHWARZ, ST. LOUIS, MO.—We have in our prenatal clinic quite frequently seen cases of marked hypotension, particularly multiparas, the hypotension becoming evident comparatively early in pregnancy.

The pregnant multipara can tell not infrequently that she is pregnant almost as much from the fact that her leg veins are enlarging, as from the fact that she has missed a period. If she has had varicosities, they become more pronounced long before any pressure could account for it. Undoubtedly there is some substance in pregnancy to which the increase in caliber of vessels is due. We also know that in pregnancy there is an increased blood volume. Considering this, we feel that perhaps the hypotension might be due to the fact that the increase in blood volume does not keep pace with the enlargement of the circulatory bed.

DR. HUGO EHRENFEST, ST. LOUIS, MO.—Both low blood pressure and slow labor have been ascribed to a deficient function of the posterior pituitary body, and it has been suggested to administer pituitary extract during pregnancy. I have never dared to try this medication but would like to know whether Dr. Williams has any experience with the continued use of pituitary extract during pregnancy to raise blood pressure and prevent a slow labor.

DR. CAREY CULBERTSON, CHICAGO, ILL.—This question of blood pressure in pregnancy has been very markedly stimulated in the last 10 or 15 years by the careful observations that have been made in association with gain in weight as a method of estimating such things as pregnancy toxemia. Accordingly we have taken blood pressure on all of our patients, and I have been impressed with the tendency toward low arterial tension throughout pregnancy in many patients.

Dr. Williams placed these patients in the two groups of the asthenic and the energetic types. It is with the asthenic patients that we have to be particularly careful. We have to guard these women in early pregnancy against further loss of weight from vomiting. They often have a bad habit of not eating, acquired long before gestation.

I had hoped that Dr. Williams in giving the blood pressures would also mention the diastolic tension, because I think that the pulse pressure is one of the best indicators of the patient's condition. Those patients with low systolic blood pressure in whom the diastolic is not correspondingly decreased are the ones who complain particularly of fatigue.

I was glad to hear Dr. Williams differentiate between the undernourished and the fat patients. We have to keep the thin patients on frequent feedings, small quantities every four hours. The tendency to toxemia in thin women is not nearly so great as in the fat patients.

DR. L. A. CALKINS, UNIVERSITY OF VIRGINIA, VA.—Has Dr. Williams controlled this asthenic group with hypotension by comparing them with another asthenic group but with normal blood pressures in relation to labor and other unsatisfactory features of the puerperal state?

DR. PHILIP F. WILLIAMS (closing).—In reply to Dr. Ehrenfest I would say that I used pituitary extract, not over a week at a time, three times a day, the patients resting most of that time in bed. It had a very slight effect on increasing the blood pressure.

In making my comparisons with other cases I unfortunately did not do as Dr. Calkins has suggested, that is, compare these cases with an equal number of asthenic women with normal blood pressures, but did compare them with a series of women, a much larger series, taken at random who did have normal pressures and concluded that the duration of labor and the degree of prematurity were considerably accentuated in the hypotensive women.

**Basal Metabolism Determination in Pregnancy**, by DR. E. D. PLASS, Iowa City, Iowa. (By invitation.) (For original article, see October issue, page 556.)

### DISCUSSION

DR. CARL H. DAVIS, MILWAUKEE, WIS.—Dr. Stander wrote a paper some years ago which showed somewhat similar results without the use of iodine, since his patients lived where sea food is prevalent. My patients all had iodine, with one exception, in somewhat larger amounts than Dr. Plass gave, and yet as far as I can follow the charts the results were more or less comparable. In other words, the patients who had perfectly normal thyroids, on the average stayed within normal limits during the period of pregnancy, whereas those who had abnormal thyroids even with iodine showed a metabolic rate above the normal.

Of greatest importance is the observation that when sufficient iodine is given during pregnancy we can practically eliminate congenital goiters. We hope that we will also greatly reduce the tendency to later development of goiter which is now so prevalent and becoming such a problem in certain parts of this country. Those of us who live in the Great Lakes district are seeing a constantly increasing number of women who have evidences of thyroid abnormality. Myxedema, cretinism, as well as the various forms of hyperthyroidism are much more prevalent with us than in other parts of the country.

I was very much interested to hear last summer in de Quervain's Clinic at Berne that, since iodized salts are being used in Switzerland, adolescent goiter has greatly decreased. He feels that the use of the iodine is going to control the problem of congenital goiter.

DR. JOSEPH P. DELEE, CHICAGO, ILL.—This fact might be of interest: By feeding cows the residue from fish factories, chiefly bones left over from canning, the iodine content of their milk can be raised to, I think, 315 parts per billion or even higher. That brings the milk up to the iodine food value of the Columbia River salmon. Experiments are now being carried on in several dairies, chiefly in the Rock River Farms near Chicago. I have been asked whether I would recommend the steady diet of such milk for pregnant women. The iodine after passing from the bones of the fish into the cow's milk, the dairymen claim, is more assimilable and palatable than the iodine obtained from sea kelp. It is also claimed that abortion in cattle has been somewhat reduced under the fish residue régime.

DR. CARL H. DAVIS, MILWAUKEE, WIS.—Some years ago I found that a few of my patients were developing hyperthyroidism within a year after delivery. Following this observation I began to have them continue the iodine during the period of lactation and since then have not had a single patient who has developed a hyperthyroid condition. Whether this is a coincidence or not I am not prepared to state, but Dr. DeLee's suggestion seems worth while.

DR. OTTO H. SCHWARZ, St. Louis, Mo.—I feel that the increase in metabolic rate during pregnancy is not entirely due to the growth of the fetus but also to increased thyroid activity, and this is particularly shown in such cases where thyroid hyperactivity exists already. Apparently Dr. Plass is not of this opinion. In pregnant animals can be observed a marked increase in the activity and a storage of colloid in the gland which disappears shortly after term or even at term. It seems to me obvious that the fetus in utero is under such a condition that its metabolism would be much less than that of a newly born child. In calculating rates of mother and newborn it is in my opinion not justifiable to take the rate of the newborn as comparable to the rate of the fetus in utero.

In view of this fact and in view of the changes of the thyroid in pregnancy, I believe that the increased metabolic rate is in a definite part due to increased thyroid activity.

DR. JOSEPH L. BAER, CHICAGO, ILL.—I published a study of basal metabolism in pregnancy and the puerperium. In that series it was attempted to eliminate any patient with an obviously enlarged thyroid or with symptoms of hyperthyroidism. Today listening to this very exhaustive study of the subject, under much more rigid control of conditions and including a precise study of the thyroid states of the patients, I am glad to see confirmed the figures obtained at that time, particularly because in the meantime two papers have appeared denying any increase in metabolism in the normal woman at the end of pregnancy.

DR. E. D. PLASS (closing).—I think that our clinical results have confirmed absolutely the work done among the lower animals relative to the protection of the infantile thyroid by the administration of iodine during pregnancy. The danger which the average internist considers a bar to the indiscriminate use of iodine has not been observable in any of our patients. We feel that one may give iodine during pregnancy, running only a very small chance of doing damage to those individuals who have adenomatous goiters.

Perhaps I did not explain clearly enough that I agree with those who say that in the perfectly normal pregnancy, with a normally functioning thyroid gland, there is no increase in the metabolic rate due to the pregnancy itself. I believe that is shown particularly by the fact that in the perfectly normal individual there is an extremely abrupt drop in the basal metabolic rate immediately after delivery. If that drop depended upon a regression in the thyroid gland, one would expect it to be slower. Its abruptness is good evidence that the increased rate in normal pregnancy is due practically entirely to the metabolic activities of the fetus in utero.

### **Important Procedures in the Conservative Treatment of Eclampsia, by**

DRS. WILLIAM J. DIECKMANN AND OTTO H. SCHWARZ, St. Louis, Mo.

(For original article, see October issue, page 504.)

### **DISCUSSION**

DR. JOHN W. HARRIS, MADISON, WIS. (by invitation).—I was quite surprised that Dr. Dieckmann reported a marked concentration of the blood in his eclamptics during pregnancy. The experimental work of Stander and Tyler, of Plass and Bogart on plasma proteins seems to show that in normal pregnancy there is a marked dilution of the blood during pregnancy with a subsequent concentration during labor, followed by a second dilution fairly early in the puerperium.

Several years ago Dr. Gray and I found that through pregnancy up to term there was a marked dilution of the blood, with a low cell volume, low hemoglobin and a high fluid volume. During labor there was a marked concentration of the blood followed promptly about the first or second day of the puerperium by a second dilution, and a gradual return to normal fairly late in the puerperium.

It has been stated that the degree of blood dilution in the toxemias of pregnancy is more or less dependent upon the tissue edema. Plass and Bogart, and Stander claim that in eclampsia the blood dilution is more marked than in the normal case.

In regard to treatment we agree with Dr. Dieckmann and Dr. Schwarz. The mild case will recover if let alone. It is in the severe cases that our results are not so satisfactory. The difficulty comes in distinguishing the severe case of

eclampsia from the mild one and determining upon operative procedure early enough before the patient becomes a poor operative risk. In this respect the work of Dr. Dieckmann and Dr. Schwarz is of great value. In the severe cases many of us are coming to believe that conservatism is no longer advisable and, as Dr. Dieckmann said, if prompt delivery cannot be accomplished through the natural passages, cesarean section is to be given serious consideration. In this connection we should take into consideration the work of Stander on the effect of anesthesia on the blood picture. He has recently shown that the experimental use of all the various types of inhalation anesthesia produces the same blood picture that is present in cases of eclampsia. This may well explain why so many of us in the past have had such bad results from cesarean section in the treatment of eclampsia. Stander has shown that even large injections of the usually employed local anesthetic do not produce these blood changes and this might well explain the relatively good results reported by DeLee in the treatment of eclampsia with cesarean. The injection of ephedrin in spinal anesthesia has been a great advance. Spinal anesthesia has the advantage that it is less disturbing to the patient and also that the operation can be done in much less time.

DR. GEORGE W. KOSMAK, New York, N. Y.—The work of Dr. Schwarz and Dr. Dieckmann, together with that done by others in recent years, is a most valuable contribution because their work has established more firmly the conservative treatment of eclampsia. I have always looked upon an eclamptic woman as a medical as much as an obstetric case and the problem of delivery in my belief is less important than that of her recovery. I am rather surprised at the comparatively large incidence of operative deliveries, five cesarean sections in a series of nineteen cases, especially since these patients presumably were studied carefully during the antepartum period. This rather high operative incidence does not seem to coincide with the other claims made for the more conservative treatment.

My own experience with magnesium sulphate has not been so satisfactory, in regard to sedative action as with morphine and scopolamine or atropine, and I therefore prefer morphine to magnesium sulphate for cases that show a tendency to convulsions.

A point that I do not believe has been sufficiently touched upon, is the condition of the patient after delivery. There seems to be a natural tendency, even where we tried to pursue conservative methods, to get these women delivered as rapidly as possible, although we may not resort to an operative delivery. The great danger for patients running high blood pressures is a sudden drop, which occurs within twenty-four hours after delivery and often results in death. The picture strikes me as one of vasomotor shock, in which there is an overfilling of the abdominal vessels. I question the advisability of giving these women large amounts of fluid intravenously. I think we get as good results from the concentrated glucose, say a 25 per cent solution, given in a dose of not over 250 c.c., and given very slowly, so that the administration of 250 c.c. may take from one to two hours, thus eliminating all shock to the circulatory system likely by the more rapid injection of large amounts of fluid. The diuretic effect of the glucose is equally as well marked. These patients do very well if on the third or fourth day they are given another intravenous infusion, particularly if they are irrational and it is difficult to give fluids by mouth.

DR. OTTO H. SCHWARZ, St. Louis, Mo.—Dr. Dieckmann has to do not only with the laboratory work, but also is responsible for the treatment of the patient as soon as she enters the hospital. He observes the patient on admission, recommends the entire treatment and does the delivery on cesarean section, as the case may be. Although this series is still small, I think in time the combination de-

scribed by Dr. Dieckmann will prove most valuable in the treatment of late toxemias of pregnancy. Our clinical experience, however, covers considerably more than 31 cases. We have a large city hospital service with a large number of referred patients, almost all severe cases, and Dr. Dorsett has treated there over 120 cases with magnesium sulphate in the last four or five years. In the first part of the series of 60 odd cases, with six deaths, he used a considerable amount of magnesium sulphate, much higher than in the latter half of the series. In the latter half, he used 1000 c.c. of 10 per cent glucose solution, at least once, and sometimes more often. He was able in this series to appreciably reduce the use of magnesium sulphate. In Dr. Dorsett's later series, there were 54 cases with five deaths, three dying undelivered. The magnesium sulphate is given intramuscularly. Dr. Dorsett also induces labor with a bag in most cases. A blood dilution has been reported in late pregnancies and more particularly in eclampsia. We were rather surprised to find a marked blood concentration in cases of eclampsia with convulsions, and therefore report this finding with emphasis.

DR. JOHN C. HIRST, PHILADELPHIA, PA.—In the University of Pennsylvania Maternity Hospital I think we have had about 148 cases of eclampsia since 1920, and in that number one patient had one convulsion and died. Another had more than 100 convulsions and survived, so that I would like to emphasize the fact that the severity of eclampsia cannot be estimated by the convulsions alone.

DR. E. D. PLASS, IOWA CITY, IA.—Dr. Dieckmann's paper gives some very definite evidence with regard to the usefulness of hypertonic glucose solutions and indicates that the good effect which is produced is largely physical and certainly not specific. There is a relationship between the amount of clinical edema and the amount of blood dilution, which seems to indicate a balance between the circulating blood and the tissues. If it is possible in any way to disturb that balance by increasing the osmotic pressure inside of the circulatory system, we tend to produce a diuresis, and it is my opinion that the beneficial effects of hypertonic glucose solution are due to their hypertonicity rather than to the fact that they contain glucose, and that they act in a purely physical way by increasing the osmotic pressure, drawing the fluid out of the tissues and putting it in a position where it can be excreted by the kidneys.

DR. E. L. KING, NEW ORLEANS, LA.—The indiscriminate use of cesarean carries with it a high mortality. We collected at one time a series of 291 cesarean sections with a maternal mortality of 42 per cent in those performed for eclampsia. In Detroit it was practically the same in a series reported there. In Brooklyn it was 26 per cent. I would like to ask the criteria on which Dr. Dieckmann and Dr. Schwarz decide to do a cesarean in any given case, and at just what time of the treatment they employ the cesarean? Do the patients get the preliminary treatment first and thereby get in better condition? Just what points are employed in determining whether to do cesarean section or to resort to some other measure?

DR. FRED L. ADAIR, MINNEAPOLIS, MINN.—It is well known that in association with eclampsia there is frequently a cerebral edema. If this use of hypertonic solution intravenously changes the osmotic pressure it undoubtedly has a favorable effect on the edema by lessening the amount of tissue fluid in the central nervous system.

DR. WILLIAM J. DIECKMANN (closing).—Dr. Kosmak spoke of our high incidence of cesarean section, 5 cases. Only 2 of these 5 patients had had prenatal care, one as a private patient and the other at a municipal clinic. One

cesarean was performed on a mild case but she was a private and not a ward patient. We have had no difficulty in controlling the convulsions, probably through the dehydrating effect on the brain of the hypertonic glucose. Cerebral edema itself does not as a rule cause convulsions, but it does predispose to convulsions. At first we used small amounts of glucose but soon found that it required about 200 gm. to be effective. We are trying to find out just what the glucose does. We know that in many cases we get a marked and permanent blood dilution and that the coma disappears. We are undoubtedly changing the osmotic balance but do not know whether by forcing chlorides out, by changes in the permeability of the capillary walls, or by some other process. We consider the convulsions only as a symptom and because of our ability to control them do not attach much significance to them.

Dr. King spoke of our criteria for cesarean section. As outlined, we believe that our procedures will in a period of eight to twelve hours either make recovery assured or convince us that something else will have to be done. For example, if after the patient has been treated for this period, coma is developing or not clearing up, if a hyperpyrexia develops, or if the urinary output remains small, then we believe the case is not only severe in type but also that delivery should be completed as safely and quickly as possible.

**Gonorrhea in the Female**, by DR. LUCIUS E. BURCH, Nashville, Tenn.  
(By invitation.) (For original article, see page 689.)

#### DISCUSSION

DR. ROLAND S. CRON, MILWAUKEE, WIS. (by invitation).—In reviewing my private records I found 17 sterility patients who had had neisserean involvement of the tubes and ovaries. In all of these the Rubin insufflation test was performed, but in only three instances was it possible to force carbon dioxide through either one or both tubes at a pressure between 160-180 mm. One of these patients later became pregnant. Complete healing of gonorrheal infection does occur, but scarring with closed tubes is the rule.

We have obtained most gratifying results by the use of the long nasal-tip cautery without splitting and resuturing the cervix. There are now available records of about 500 patients, cared for at the Milwaukee County Hospital under the supervision of Dr. Shutter and others, in whom a vast majority of cures have been obtained. Repeated cauterizations, sometimes carried well into the internal os, may be necessary.

Bartholin's and Skene's glands are frequently involved and, notwithstanding Dr. Burch's statement, they frequently call for eradication. The cauterization of Bartholin's ducts and glands is at times very unsatisfactory. In general, it is probably better to excise the gland, especially when it is one of the shot-like enlargements.

Skene's glands may be located laterally or in the base of the urethra and vary from approximately  $\frac{1}{4}$  inch in length to over one inch. The glands of Morgagni or Littre may also become involved. Only in Graves' book Schuller's duct located in the top of the urethra is mentioned, and in this particular patient measured over one inch in length. Infection of all of these glands frequently calls for treatment, either irrigation with a blunt cannula syringe, sometimes cautery, but best of all incision or splitting.

DR. GUY L. HUNNER, BALTIMORE, MD.—Textbooks invariably speak of the great rarity of gonorrheal infection of the bladder. I suppose these statements are based largely on early experience with the male, in whom one cannot justifiably

investigate the bladder to find out whether he has a gonorrheal infection. In the female it can be done without damage. If a female has a urethritis during acute gonorrhea, she usually has cystitis as well. One can prove that by finding in a catheterized specimen the pus cells crowded with gonococci, or growing them on special media, or by discovering through the cystoscope the typical gonorrheal ulcers distributed over the surface of the bladder. In tuberculosis we often see a tiny linear, brilliant red ulcer which we have learned to interpret as suggestive of tuberculosis, but the elusive ulcer frequently duplicates this picture. In the acute gonorrheal bladder we usually find a fairly normal pale pink background, and on this are from one to a dozen or more areas characterized by a tiny red center to which radiate many congested vessels with almost the uniformity of the spokes of a wheel. With the constant irrigation which the urine affords, and the relatively weak resistance of the gonococcus, the picture soon disappears.

Our dealings with the gonorrheal bladder usually occur after the gonococcus has departed from the bladder, and possibly from the urethra, but has left those toxic effects on the nerve endings in the trigonum and urethra which result in a chronic state of trigonitis and urethritis, often difficult to diagnose from the identical cystoscopic picture caused by distant foci of infection. We might be helped in the diagnosis by the typical history in the gonorrheal case, or by the history of a distant focus of infection. The silver nitrate treatment usually acts like magic in the gonorrheal case, and yields little or no results in the focal infection case which is cleared up only after discovering and removing the distant focus.

Dr. Burch's method of treating endocervicitis seems too radical, but I agree with his conservatism in treating the intrapelvic gonorrheal conditions. We can get permanent results in most of the endocervicitis cases with the various cautery methods used in the office without general anesthesia.

DR. JOHN A. McGLINN, PHILADELPHIA, PA.—When Dr. Burch published his first paper, I did the operation as he originally described it, laying open the cervix with a cautery and then packing it with mercurochrome gauze. Frankly, I was disappointed with the operation, as I could accomplish the same ends by an easier method. The operation as he shows it today is a distinct improvement over the original one.

We have used practically all the methods which have been proposed at one time or another for the cure of gonorrhea. We followed very carefully the Corbus method in two hospitals and were not able to obtain a sufficient number of cures to continue the procedure. We have used all sorts of lights, diathermy and injections into the cervix, various antiseptics, vaccines and even intravenous injections of mercurochrome, and have come to the conclusion that the best way to eradicate gonorrhea from the cervix is by the proper use of the cautery.

Dr. Morrison, one of my assistants, following the work of Pelouze in gonorrhea of the prostate, has added massage to cauterization in the treatment of gonorrhea of the cervix. We believe that our results are better since we have been using this combined method.

DR. LUCIUS E. BURCH (closing).—I gave linear cauterization a thorough try-out before using the present method and discovered that I was unable to effect a cure.

Diathermy and topical applications to the endocervix were ineffective in my hands. If any of you will only once thoroughly dilate a cervix and then incise it and see the large amount of mucous membrane contained in the endocervix, you will quickly realize how futile linear cauterizations and topical applications are for relief of gonorrheal endocervicitis.

In effecting a cure the whole endocervix must be cauterized. I formerly advised the application of antiseptics to the endocervix following the incision of the



cervix. This is an unnecessary step with the present technic. The operation is not difficult and hospitalization is short unless large masses are present.

Dr. Hunner has presented some very valuable information concerning gonorrheal ulcers of the bladder, but even here the gonococcus does not survive after the ulcer has formed.

Dr. McGlinn brought out the difficulty of ascertaining when a case was cured. I believe one is safe in considering a patient well when negative smears are obtained after three successive monthly periods following the operation. Alcohol or whisky given orally bring gonococci to the surface but not so well as the monthly period.

**The Pathologic Diagnosis of Early Uterine Cancer With Especial Reference to Its Differentiation From Pseudo-Malignant Inflammatory Lesions, by DR. EMIL NOVAK, Baltimore, Md. (For original article, see October issue, page 449.)**

#### DISCUSSION

DR. GEORGE GRAY WARD, NEW YORK, N. Y.—Two things strike me as very important to be borne in mind from the clinician's standpoint. First, it is a complicated matter requiring great judgment and experience to make a correct diagnosis in many of the cases which are submitted for an opinion. We are seeing more and more of these early cases because the women are being educated as well as the doctors, and we not infrequently have to ask the pathologist for a diagnosis. Biopsy and curettage in the fundus cases we can do without much fear of dissemination of the disease. As to relying on frozen sections, my pathologist, Dr. Plaut, feels that this is not safe, and we are using paraffin sections which take a few hours, but yet not so long as the routine method. In doubtful cases we might put in the radium. We will get a report in a very few hours so that if the case is not malignant the radium can be removed after only a small dosage has been administered.

The importance of curing all diseased cervices is very apparent if these cases are prone to go on to cancer. Dr. Novak justly emphasizes that we have been in the past entirely too prone simply to give the specimen to our pathologist and let his word be final. It seems to me that we should be just as particular in selecting the pathologist for consultation as we are in the selection of consultant in cases of questionable operation. We have had recently quite a few cases where there has been some question as to diagnosis, though the pathologist was fairly sure, and I have insisted that these specimens be taken to Dr. Ewing for another opinion. We should employ consultation with the pathologist more frequently than we do.

Within the past few weeks a woman came to me with a small cyst of the left ovary which was densely adherent and very painful. The patient was a young married woman in the twenties. Last summer a surgeon in New Brunswick had removed a right ovarian cyst. The pathologist made the diagnosis of sarcoma of the ovary and said the other ovary as well as the uterus must be taken out. Before doing anything I got the slides from New Brunswick and after they were passed upon by my pathologist and another pathologist in New York it was decided that there was absolutely no sarcoma, and we were able to save the other ovary.

DR. ARTHUR H. CURTIS, CHICAGO, ILL.—I have spent a very material part of my medical life in the laboratory. Looking at this subject from the point of view of a laboratory worker, as well as that of a clinician, I would emphasize

most forcefully that laboratory study is merely a corollary to clinical work. The fundamental thing about a diagnosis of early cancer of the cervix is an adequate knowledge of gross pathology. With a good light over our shoulder we should bring down the cervix by "delivery of the uterus" so that we can see the cervix perfectly in doubtful instances, splitting the anterior lip for a better view of the endocervix when necessary. (I have very much less hesitancy about cutting into doubtful tissue than most of you.) The ideal thing, of course, is to take out all of the diseased portion of the cervix rather than remove only small pieces for study.

Let us not leave too much to the laboratory diagnosis. I believe thoroughly in a microscopic study; its value is irrefutable, but we must not place notable dependence upon modern refinements in histopathology.

As to cutting into cancerous tissue, I do fear it; but I think *the most important thing in the spread of cancer is the manipulation and the squeezing of the diseased tissues*. Such procedures in a doubtful case forces into the adjacent tissues a good deal more material than does one clean cut with the knife.

DR. WILLIAM P. GRAVES, BOSTON, MASS.—I cannot agree with Dr. Curtis in the matter of relying on gross inspection for the diagnosis of cancer of the cervix, and in order to illustrate the importance of biopsy to detect the disease, I will relate an experience which I have already reported.

We have always believed that the repair of a lacerated cervix is an effective though not a perfect preventive of a later cancer. In order to obtain some real information on this point, we made an investigation of all our cervical repair cases, amounting to nearly six thousand. When it was found that a patient had developed a cancer after a trachelorrhaphy, the specimen of tissue removed at the repair operation was subjected to a searching reexamination. In 3 cases it was discovered that the unsuspected cancer in an early stage had actually existed and had been overlooked by an experienced pathologist in his routine examination of the tissue removed. In all three cases the cancerous disease did not make itself known until three or four years after the repair operation.

No better evidence than this could be adduced to support Dr. Novak's insistence on the vital importance of searching expert biopsies in the diagnosis of cervical cancer.

DR. N. S. HEANEY, CHICAGO, ILL.—Does Dr. Novak recommend that a piece of the suspected area be taken out for examination? Is that what he means by a biopsy? If this is his recommendation, I disagree with it. If there is a visible lesion, the cervix should be amputated so as to include all the suspected area and an examination made after its removal. If it is cancerous, proper therapy can then be carried out, and the patient has not been jeopardized by having the area cut into. If it is not malignant, the patient is free of her lesion and relieved of her complaint. I think too many men turn the tissue over to a pathologist and abide by his decision so they never learn to correlate their clinical and pathologic experiences. This, of course, is not Doctor Novak's way of doing things, but it is true in too many places, and of necessity under such circumstances suspicious areas are diagnosed only on their microscopic appearance when most of them should have been diagnosed on their gross appearance.

DR. CAREY CULBERTSON, CHICAGO, ILL.—We should remember that Dr. Novak's remarks have been limited to that relatively small group of cases where the diagnosis is not evidently clear on gross inspection. I have not reached that point of visual accuracy where I am satisfied on looking at these small lesions of the cervix to say whether they are malignant or not. I am rather strong for biopsy, the excision of a piece of tissue and a speedy microscopic diagnosis of it. I have always followed my work into the laboratory. I had a very good lesson

in that some years ago at the county hospital in a case of evident incomplete abortion. The tissues went in the routine way to the laboratory, and the pathologist at that time was a relatively young and inexperienced man to be sure. He did not see any chorionic villi and sent back a diagnosis of malignant embryonic squamous carcinoma. Of course, he saw the embryonic epithelial cells. To leave the matter always to the pathologist is not by any means satisfactory. These cases of "atypical cellular proliferation," which is a nicer phrase to use than precancerous because it does not make the pathologist so angry, are precancerous I believe. I think that they represent a cellular proliferation, but sometimes they are very markedly obscured by round cell infiltration and are not as distinct as those Dr. Novak showed us today. And those are the ones, too, in which there is necessarily considerable doubt.

Dr. Novak referred to the propaganda. Cancer propaganda is aimed at the laity, and he intimated that it should as well be aimed at the general practitioner. That is without any question correct. I teach my students in the laboratory that it is up to the first doctor who sees the case to make the correct diagnosis, and for this the biopsy is essential.

DR. JOSEPH P. DELEE, CHICAGO, ILL.—May I ask Dr. Novak to tell us something about Hinselmann's work on the leucoplakia of the cervix, and what he thinks of it?

DR. HERMAN J. BOLDT, New York, N. Y.—I wish to emphasize most strongly the statement of Dr. Ward, that it is important occasionally to call the pathologist into consultation.

I have made it a rule to have every specimen examined and have seen three instances where a carcinoma was discovered that had not even been suspected. On two other occasions where competent men in our own city had made the diagnosis of carcinoma, but for clinical reasons I had some doubt about it, I sent the specimens to Dr. Welch of Baltimore. He returned a long report as to why the diagnosis of carcinoma was made but why it was not carcinoma.

DR. FRED L. ADAIR, MINNEAPOLIS, MINN.—A number of years ago I studied the healing process of cervical erosions. The squamous epithelium was seen invading the glands and undermining the surface and glandular epithelium, producing these very confusing pictures.

In the Middle West they have in many hospitals laboratory pathologists who are not particularly well trained in tissue diagnosis, and I know of serious mistakes which could have been avoided by consultation with an expert pathologist. We must keep in mind that not all doctors are experts in gynecologic diagnosis and for them a biopsy is probably the safest means of arriving at an accurate diagnosis.

DR. F. A. PEMBERTON, BOSTON, MASS.—Having seen many slides of different diseases of the cervix, we believe the gynecologic pathologist is in a better position to judge about these doubtful cases microscopically than the general pathologist, and Dr. Mallory agrees with us.

DR. EMIL NOVAK (closing).—Like Dr. Ward, I feel that the danger of disseminating cancer cells by biopsy upon the cervix is not very great. Furthermore, even if there were some danger, we would, when indicated, do it anyhow, for there is no other way yet available to settle the diagnosis in the doubtful case. The same statement can be made with regard to diagnostic curettage.

Dr. Curtis is inclined to minimize the frequency of cervical lesions in which a careful clinical examination does not suffice to establish the benign or malignant

nature of the condition. Perhaps, as with so many other questions, a compromise between the viewpoint of Dr. Curtis and myself may reflect most nearly the attitude of most gynecologists. While I agree that in the great majority of cases a careful clinical examination is all that is necessary, and that in such cases a biopsy is not necessary, nevertheless I am sure that in my own work I have seen a considerably larger number of exceptions than Dr. Curtis estimates from his own probably considerably larger material. In the ordinary cervical erosion, with smooth, nonvascular surface, biopsy is certainly not necessary. Nor is it necessary, except for confirmation purposes, to do biopsy in the frank cancer. The total number of cases in which biopsy is necessary, therefore, is not very large, the proportion being only a few per cent of all the cervical lesions observed.

Dr. Graves has mentioned a number of cases in which cancer was demonstrated microscopically, although there was apparently no clinical suspicion of malignancy. In our own laboratory I can recall at least 2 cases in which trachelorrhaphy was done by expert gynecologists for lesions later shown to be cancerous. In my paper I presented the results of follow-up studies made by a number of investigators, showing that the microscope will not infrequently belie the clinical impression, and that the subsequent course of the patient is in accord with the microscopic diagnosis. Our own results are in accordance with these general findings.

Cancer of the cervix is only rarely revealed by pathologic examination when there is no clinical suspicion whatever of cancer. But it is not infrequently found where the lesion clinically is only suspicious. Furthermore, and this is just as important, the microscope will often show complete absence of cancer in cases which clinically must be regarded as very suspicious.

Dr. DeLee inquires about the incidence of leucoplakia in the cervix. Hinselmann has recently written much about this lesion, but we have not been able to convince ourselves that it is at all common on the cervix if we understand by leucoplakia what the term conveys in relation to the vulva or to the tongue.

# Department of Reviews and Abstracts

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CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

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## Collective Review

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### The Interrelationship of the Anterior Hypophysis and the Ovaries

#### A REVIEW OF THE RECENT LITERATURE

BY C. F. FLUHMANN, M.D., C.M., SAN FRANCISCO, CALIF.

*(From the Department of Obstetrics and Gynecology, Stanford University School of Medicine)*

THE recent advances in our knowledge of the physiology of the anterior hypophysis and its relation to the female genital organs have served to open a field of investigation which is of the utmost importance to the gynecologist and the obstetrician. The purpose of this review is to consider some of the outstanding reports of experimental work dealing with the interrelationship of the anterior pituitary body and the ovaries, and with the preliminary attempts at a clinical application of these findings.

In order to classify the work that has been done on this very complicated problem, it may be advantageously considered under a number of headings. (1) Effects of hypophysectomy. (2) Effects of the administration of anterior hypophyseal extracts. (3) Effects of the transplantation of fresh anterior pituitary gland tissue. (4) Is there more than one anterior pituitary hormone? (5) The Zondek-Aschheim test for anterior pituitary hormone. (6) The anterior pituitary gland during pregnancy. (7) The anterior hypophysis following castration. (8) Relation to gynecologic disease and therapeutic possibilities.

#### EFFECTS OF HYPOPHYSECTOMY

The operation of hypophysectomy, which has been performed many times on experimental animals, chiefly dogs, is followed by profound alterations of the genital organs. As a result of total or partial removal of the anterior lobe of the hypophysis the most striking feature is a state of adiposity accompanied by (or resultant to) a secondary hypoplasia of the organs of generation in adults, or by a persistence of sexual infantilism in case the primary hypophyseal deficiency antedates adolescence (Crowe, Cushing and Homans<sup>1</sup>; Aschner<sup>2</sup>; Smith<sup>3</sup>; Reichert<sup>4</sup>). The destruction of the pituitary gland by the injection of a chemical substance also results in marked disturbances in the reproductive system (Smith, Walker, and Graeser<sup>5</sup>).

## EFFECTS OF ADMINISTRATION OF ANTERIOR HYPOPHYSEAL EXTRACTS

Previous to 1921 there had been many attempts to obtain a promotion of growth and the stimulation of the ovaries of laboratory animals with various preparations of the anterior pituitary lobe, and although one or two successful results were described, the evidence on the whole was not conclusive and many experimenters reported negative findings. Both fresh glands and extracts were employed and administered either by injections or by feeding to dogs, rats, or guinea pigs. Sandri,<sup>6</sup> Aldrich,<sup>7</sup> Lewis and Miller,<sup>8</sup> R. T. Frank,<sup>9</sup> Sisson and Broyles,<sup>10</sup> Kross,<sup>11</sup> and C. S. Smith,<sup>12</sup> were unable to produce any effects on body growth and gonad activity, while Goetsch<sup>13, 14</sup> and Marinus<sup>15</sup> claimed to have obtained a stimulation of both these factors. Clark<sup>16</sup> maintained that he was able to stimulate the ovaries in hens, as evidenced by increased egg laying, by feeding fresh anterior pituitary gland, but on the other hand this was denied by Pearl and Surface<sup>17</sup> and Pearl<sup>18</sup> who failed to corroborate the finding either by the injection or by feeding of a desiccated preparation. Both Evans and Long<sup>19</sup> and Smith<sup>20</sup> have also reported negative results from feeding fresh gland tissue.

In 1921, Evans and Long<sup>21, 22</sup> succeeded in producing very definite changes in the reproductive system of the white rat by the intraperitoneal injection of an alkaline preparation of bovine anterior hypophyseal substance. They found that estrus in these animals was absent or was exhibited at long intervals. The uterus remained infantile, but the ovaries were twice the size of those of the control animals. Histologic examination showed the presence of very abundant lutein tissue in the ovaries and the formation of this tissue about the egg in unruptured normal follicles and in atretic follicles. Ripe, normal graafian follicles were invariably absent. A powerful, specific stimulus to lutein cell transformation was thus effected by this hormone. These findings were confirmed by Brouha and Simonnet,<sup>23</sup> and Walker<sup>24</sup> was able to inhibit ovulation in the domestic fowl by the intraperitoneal administration of anterior hypophyseal substance. Teel,<sup>25</sup> Brouha,<sup>26</sup> and Evans and Simpson<sup>27</sup> were also able to bring about a decidual cell response to injury of the uterine mucous membrane (the "placentoma reaction") by the use of daily injections of similar extracts.

## EFFECTS OF THE TRANSPLANTATION OF FRESH ANTERIOR PITUITARY GLAND TISSUE

Although a number of attempts were made to obtain results by the introduction of fresh living gland tissue by transplantation (Klinger,<sup>28</sup> Hofstätter,<sup>29</sup> Schäfer,<sup>30</sup> Clairmont and Ehrlich,<sup>31</sup> Exner<sup>32</sup>) negative findings were reported, until Smith<sup>3, 33</sup> in 1926 used daily transplants of anterior lobe in an attempt to overcome the effects of hypophysectomy in the white rat. He found that not only was he able to restore an almost normal growth rate, but in addition there was a partial repair of the injury to the sex glands. Smith<sup>34, 35, 36</sup> and Smith and Engle<sup>37, 38, 39</sup> extended the study of anterior pituitary transplantations and succeeded in inducing a precocious sexual maturity in very young rats and mice. Transplants were made once or twice daily, and with striking rapidity the vaginal introitus became established and the vaginal smear revealed an estrual condition. At autopsy the sex organs of these animals showed a tremendous hypertrophy, the ovaries

gave evidence of ovulation, and ova were found in the fallopian tubes. The vaginal and uterine changes could not be obtained in spayed animals, and transplants from immature or senile, male or female animals, and from rats, mice, rabbits, guinea pigs, and cats were effective. It was thus shown that fresh anterior pituitary transplants act as a powerful stimulus to normal ovarian function, a finding in direct contradiction to the results obtained by Evans and Long with their alkaline extract.

Zondek and Aschheim,<sup>40, 41, 42</sup> working independently of, and simultaneously with, the above authors, also succeeded in producing precocious sexual maturity in young mice by similar transplantations of anterior pituitary tissue. They found that the glands obtained from immature, mature, or senile animals were effective, as were those from human subjects and from cattle. These workers assert that the anterior pituitary body is the active *motor* agent that stimulates the ovary to activity, and that the resultant changes in the uterus and vagina are due to the effect of the ovarian follicular hormone thus produced.

This outstanding work of Smith and Engle, and Zondek and Aschheim has received abundant confirmation from numerous sources, for example, Fels,<sup>43</sup> Biedl,<sup>44</sup> Ehrhardt,<sup>45</sup> Siegmund,<sup>46</sup> Lipschutz and Paez.<sup>47</sup> In addition, a number of experimenters have used different species of animals as recipients of the transplants with equal success. Allen<sup>48</sup> was able to induce precocious sexual maturity in monkeys, Reiss and Langendorf<sup>49</sup> in dogs and rabbits, Riddle and Fleming<sup>50</sup> in ring doves, and Wolf<sup>51</sup> produced ovulation in frogs. Grueter<sup>52</sup> used an aqueous extract of the anterior pituitary gland and also obtained an ovarian response in rabbits. Engle<sup>53</sup> has shown that the anterior pituitary gland is an important factor in the compensatory hypertrophy of the ovary which occurs after unilateral or subtotal ovariectomy, and also that grafted ovaries respond to transplants.<sup>54</sup> Reichert<sup>4</sup> was able to overcome in a large measure the disabilities arising from hypophysectomy in a six weeks' old female puppy by four months of replacement therapy with daily fresh heterotransplants of rabbit pituitary gland. During this whole period external signs of estrus were present in this puppy although the littermate control did not come into heat until much later. The gonad-stimulating hormone has been found in the anterior pituitary gland of senile human beings (Schultze-Rhonhof and Niedenthal<sup>55</sup>), and of the human fetus (Siegmund and Mahnert,<sup>56</sup> and Schultze-Rhonhof and Niedenthal<sup>57</sup>), although Hauptstein<sup>58</sup> failed to corroborate the latter result.

In the light of this work there has been very little contradictory evidence brought forward. Fellner<sup>59</sup> does not believe that the ovarian response in immature animals is due to a specific hormone from the anterior lobe and states that he obtained the same result with an ovarian hormone preparation ("Feminin"). This is, however, altogether against the experience of many workers who have failed to find any changes in the ovaries following the injection of ovarian follicular hormone. Fels,<sup>43</sup> Siegmund,<sup>46</sup> and Mahnert<sup>60</sup> claim that the corpora lutea resulting in the ovaries are not true physiologic structures but abnormal formations such as described by Evans and Long and that normal ovulation thus does not take place. In this regard attention must be directed to the finding of ova in the fallopian tubes of the test animals by Smith and Engle and Zondek and Aschheim.

Some doubt has been advanced as to whether a true precocious maturity is really induced in these immature animals (Siegmund,<sup>46</sup> L. Seitz<sup>61</sup>) and Seitz suggests that we should consider it as a morphologic change rather than a true functional result. He quotes Ehrhardt as having placed a number of these artificially matured young mice with males and pregnancies did not occur any sooner than in the untreated controls. He thus feels that the assumption that the anterior pituitary gland is the activator of sexual function must be accepted with limitations.

#### IS THERE MORE THAN ONE ANTERIOR PITUITARY HORMONE?

It is thus seen that a number of seemingly contradictory effects have been induced in the ovaries of immature mice by the administration of various substances considered as originating from the anterior hypophysis. In the first place, we find the stimulation of normal ovulation with a hastening in the appearance of estrus such as obtained from the implantation of the fresh living gland; and second, an abnormal process in which there is an extensive luteinization of follicles and an inhibition of estrus, such as results from the alkaline extract of Evans and Long.

Evans and Simpson<sup>62</sup> have advanced a theory, based on experimental evidence, which seeks to explain these changes by attributing two hormones to the anterior hypophysis. There is first a "growth hormone," which is closely related to the eosinophilic cells of the pars anterior, and a "gonad-stimulating hormone" corresponding to the basophilic cells. These two substances are antagonistic to one another and the effects of the second on the sexual system can be completely nullified by simultaneous administration of the first. The anterior pituitary extract which Evans and Long used in their original experiments thus contained large amounts of the growth hormone which delayed the onset of puberty by the formation of extensive luteinization of follicles, while the implantations of the fresh gland yield mostly the gonad-stimulating hormone and produce normal ovulation.

Bellerby<sup>63</sup> also believes that there are two anterior pituitary hormones which affect the pelvic organs, namely, an "estrus-producing" and an "estrus-inhibiting" hormone, while Aschheim<sup>64</sup> goes still further and attributes three hormones to the anterior hypophysis—first, the growth hormone, second, the luteinization hormone, and third the ovulation hormone.

#### ZONDEK-ASCHEIM TEST FOR ANTERIOR PITUITARY HORMONE

On the basis of the results obtained from implantations of the anterior pituitary gland, Aschheim and Zondek<sup>65, 66</sup> have evolved a test for the hormone which promises to be of considerable clinical importance. The substance to be examined is injected into an immature mouse and in a positive test evidence of estrus (vaginal smear; hypertrophy of the uterus) is observed in about 100 hours from the time of the first injection. The animal is then sacrificed and serial sections of the ovaries are carefully examined for one or more of the following changes:

APR I. (Anterior Pituitary Reaction One)—The presence of ripening graafian follicles or of recent corpora lutea.



APR II. The finding of "Blutpunkte," small reddish pinpoints grossly visible in the ovaries and representing hemorrhages into normal and abnormal follicles.

APR III. The occurrence of lutein cell transformations in follicles and the formation of corpora lutea in which ovulation has not occurred and the ovum remains imprisoned (pseudocorpora lutea; corpora lutea atretica).

The finding of any one of these changes is considered as positive for anterior pituitary substance, but it is of interest to note that the first reaction compares to that resulting from the implantation of fresh anterior pituitary gland, whereas the third reaction was obtained by Evans and Long with their alkaline extract of bovine gland. The differentiation between the hormone of the anterior hypophysis and the ovarian follicular hormone is readily made since the former produces ovarian changes but does not act in spayed animals, while the latter never affects the ovaries and its injection in castrates causes vaginal changes corresponding to estrus (Allen-Doisy test).

Kraus<sup>67</sup> has described an improvement in the technic of the test which allows the examination of the mice ovaries without resorting to microscopic sections.

The test has been used mainly, and with success, as a means of diagnosing early pregnancy from the examination of patients' urine, but for this purpose Zondek and Aschheim insist that either reaction II or III must be present. With this means they examined 197 specimens of urine from 161 women with normal pregnancies, 68 of whom were in the first eight weeks of gestation, and obtained positive results 193 times. The control series included various gynecologic conditions and yielded 254 negative results out of 258 specimens of urine. Similar success has been reported by Louria and Rosenzweig,<sup>68</sup> Ehrhardt,<sup>69</sup> Wermbter and Schultze,<sup>70</sup> Brühl,<sup>71</sup> and Kraul and Rippel.<sup>72</sup>

In addition, Aschheim and Zondek<sup>73, 74</sup> have shown the presence of anterior pituitary hormone in the decidua graviditatis of the first four months, in the corpus luteum graviditatis, in the placenta and in maternal blood after the second month of gestation, in blood from the umbilical cord, and in the tubal mucosa of both intra- and extrauterine gestations of two months' duration. Fels<sup>43</sup> found anterior pituitary hormone in the blood serum of thirty out of thirty-eight pregnant patients. Fluhmann<sup>75</sup> obtained APR I 8 times and APR II or III 27 times with the blood serum of forty-eight women with uncomplicated pregnancies. Although the hormone is not present in the spinal fluid during normal pregnancy, positive results have been obtained in eclampsia (Ehrhardt quoted by Seitz<sup>61</sup>).

Although it is claimed to be of no value for the diagnosis of pregnancy, the presence of APR I may eventually prove of clinical assistance in the study of certain functional disturbances. Zondek and Aschheim<sup>66</sup> found it in the urine of one normal woman, in one case of acromegaly, in two cases of myxedema, in one case of hyperthyroidism, in two cases of severe pelvic inflammation, in one case of amenorrhea associated with a papillary cystadenoma, in three cases of functional amenorrhea, and in seven cases of genital carcinoma. Ehrhardt (L. Seitz<sup>61</sup>) also found it in the urine of women with amenorrhea, in certain cases of endocrine disturbances, and following bilateral oophorec-

tomy. Fluhmann<sup>76</sup> obtained positive results from the blood serum of patients following bilateral oophorectomy or radiation castration, and in several women with functional amenorrhea or irregular menstruation.

#### THE ANTERIOR HYPOPHYSIS DURING PREGNANCY

In 1898, Comte<sup>77</sup> described a gross enlargement of the anterior lobe of the pituitary gland during pregnancy, and further observations were reported some years later by Launois and Mulon<sup>78</sup> and Launois.<sup>79</sup> It remained for Erdheim and Stumme<sup>80</sup> to show that this hypertrophy is accompanied by definite histologic changes; namely, a marked increase in the number of "Hauptzellen." This finding in the human being has been corroborated by a number of other observers (Kolde,<sup>81</sup> Creutzfeld,<sup>82</sup> Mayer,<sup>83</sup> Naegeli<sup>84</sup>), and studies extended to animals have shown similar changes (Guerrini,<sup>85</sup> Morandi,<sup>86</sup> Naegeli,<sup>84</sup> Kolde,<sup>81</sup> Berblinger,<sup>87</sup> Schenk,<sup>88</sup> Lehmann<sup>89</sup>).

The occurrence of a pituitary hypertrophy during pregnancy offers an interesting physiologic problem, and although its exact significance is not appreciated, it is possibly a direct effect of ovarian follicular hormone, which is present in large amounts in the blood during the course of gestation. The "pregnancy changes" of the anterior hypophysis were produced in nonpregnant, castrated and noncastrated female animals by the injection of placental extracts by Berblinger,<sup>87</sup> Adachi,<sup>90</sup> and Lehmann,<sup>89</sup> by parabiosis experiments with pregnant and nonpregnant rats by Matsuyama,<sup>91</sup> and recently by the direct administration of ovarian hormone by Baniecki.<sup>92</sup>

In this connection the effect of transplantations of anterior pituitary gland tissue into pregnant rats and mice is of importance. It has been found that although these treatments invariably produce an abortion (Ehrhardt and Wiesbader<sup>93</sup>) especially if given during the first two-thirds of the period of gestation, ovulation may be induced in spite of the fact that the animal is pregnant (Zondek and Aschheim,<sup>94</sup> Engle and Mermod,<sup>95</sup> Fels<sup>96</sup>). Siegmund,<sup>46, 97</sup> however, states that he failed to produce changes either in the vaginal epithelium or in the sex glands by implants of anterior pituitary lobe in pregnant mice. Teel,<sup>98</sup> by the administration of an anterior hypophyseal extract, was able to lengthen the gestation period of rats from two to six days, although he found that term fetuses invariably died in utero. Evans and Simpson<sup>99</sup> believe that the interference with pregnancy is due to the extensive formation of lutein tissue in the ovary.

#### THE ANTERIOR HYPOPHYSIS FOLLOWING CASTRATION

The hypertrophy of the anterior hypophysis following total extirpation of the ovaries was first found in animals by Fichera<sup>100</sup> in 1904, and it has since been corroborated by Zacherl,<sup>101</sup> Schleidt,<sup>102</sup> Trautmann,<sup>103</sup> Kolde,<sup>81</sup> Schönberg and Sagakuchi,<sup>104</sup> van Wagenen,<sup>105</sup> Lehmann,<sup>106</sup> Berblinger,<sup>87</sup> Livingston,<sup>107</sup> Schenk,<sup>108</sup> and others. In 1908, Tandler and Gross<sup>109</sup> demonstrated an enlargement of the sella turcica of eunuchs by means of x-ray studies, and Kon,<sup>110</sup> Kolde,<sup>81</sup> and Rössle<sup>111</sup> have shown that castration in the human being results in a gross hypertrophy of the anterior hypophysis which histologically is due to an increase in eosinophilic cells and the appearance of a much-debated type of cell, the "castration cell." It is probable that these changes are accompanied by a progressive storage of the

hormone in the gland (Evans and Simpson<sup>112</sup>) and this is further borne out by the fact that the use of anterior pituitary gland implants from castrated rats provokes reactions in the ovaries of the test animals many times greater than similar implantations of normal hypophyseal tissue (Engle,<sup>113</sup> Evans and Simpson<sup>114</sup>). It is also of interest to note that following total extirpation of the ovaries in women there is a large amount of anterior pituitary hormone in the blood which is readily demonstrable by the Zondek-Aschheim test (Fluhmann<sup>76</sup>).

#### RELATION TO GYNECOLOGIC DISEASES AND THERAPEUTIC POSSIBILITIES

The successful clinical application of anterior pituitary therapy in gynecology is dependent on a number of factors: (1) A proper understanding of the exact relation of the anterior hypophysis to the pelvic organs of the human being in both health and disease; (2) the development of an active, standardized, economical preparation of the gland which is easy of administration; (3) an exact knowledge of its action on the female sex organs under physiologic conditions; (4) the determination of the correct indications for its use in pathologic states; and (5) the estimation of the proper dosage.

Although there is little known regarding the rôle of the anterior pituitary gland in the common pelvic diseases which gynecologists are called upon to treat, it is well recognized that a depression of sexual function is a symptom common to both the hypopituitary and acromegalic syndromes. Dott and Bailey<sup>115</sup> found a marked constancy of amenorrhea as the earliest evidence of a hypopituitary condition, and noted its presence in numerous instances of hypopituitary function. This fact may explain the presence of large amounts of the hormone in the blood or urine of certain amenorrheic patients (Zondek and Ashheim,<sup>66</sup> Ehrhardt,<sup>61</sup> Fluhmann<sup>76</sup>). The occurrence of a "pituitary" type of menstrual disturbance (amenorrhea, scanty or irregular menses, dysmenorrhea), accompanied by such features as adiposity, skeletal changes, and hypoplasia of the genital organs, has also been described (Fraenkel and Geller,<sup>116</sup> Klawns<sup>117</sup>). There is very little information available regarding ovarian pathology in acromegalic patients, but in one case Cushing and Davidoff<sup>118</sup> report that they were unable to find lutein cell formations such as have been observed in experimental animals. They noted, however, a striking absence of corpora atretica although the ovary contained fully developed graafian follicles. Wagner<sup>119</sup> found luteinized cysts in the ovaries of a patient with a hypophyseal tumor who had had a period of four months' amenorrhea. Ashheim<sup>120</sup> has drawn attention to the lutein cysts in the ovaries of patients with hydatidiform mole and chorioepithelioma malignum, and thinks the anterior hypophysis may prove to be an important factor in such cases. In one instance he found large amounts of anterior pituitary substance in the blood and urine.

A number of reports have been published regarding attempts to obtain a preparation of the anterior pituitary hormone for clinical use. Zondek,<sup>121, 122, 123</sup> Biedl,<sup>124</sup> and Siebke,<sup>125</sup> have obtained an active substance from the urine of pregnant patients. Putnam, Teel and Benedict,<sup>126</sup> and R  th, Hirsch-Hoffman and Walk<sup>127</sup> have prepared potent extracts from the gland itself. Ehrhardt and Wiesbader<sup>128</sup> have used subcutaneous implantations of bovine anterior hypophysis.

The effects in the human being of such preparations are not as yet

clearly understood, but a number of important observations have been recorded (Zondek,<sup>121, 122, 123</sup> Ehrhardt and Wiesbader,<sup>128</sup> Ehrhardt,<sup>129</sup> Biedl,<sup>124</sup> Hirsch-Hoffman<sup>130</sup>). The most outstanding results reported are: a tremendous congestion of the pelvic organs; an increase of the temperature of the vagina and rectum; a shortening of the menstrual cycle and a hastening of ovulation. Uterine bleeding has resulted in certain cases of prolonged amenorrhea, but as it has been pointed out, it does not necessarily follow that this represents a true menstruation, and it may well be a metrorrhagia consequent upon the intense pelvic congestion. Ehrhardt and Wiesbader, however, found a premenstrual swelling of the mucosa in a patient with dystrophia adiposo-genitalis who had had a previous period of six months' amenorrhea, and Zondek has made similar observations in other instances. Kaufmann<sup>131</sup> has found an increase of blood cholesterol after the administration of Zondek's preparation.

R. Schroeder (Siebke<sup>132</sup>) has stated two clinical tests for the determination of the effect of such a hormone in patients and particularly in cases of amenorrhea of long standing; first, the stimulation of the uterus, as evidenced by its enlargement, turgor, etc., and second, the so-called "tempo-test," which is positive when as a result of hormone treatment, follicle ripening, ovulation, and corpus luteum formation (also evidenced by the changes in the endometrium) occur in proper sequence. Siebke<sup>132</sup> is treating, with some success, four main groups of patients, (a) those with too frequent menstrual bleeding, (b) with prolonged menstrual cycle, (c) with absence of menstruation, and (d) with hypoplastic genitalia accompanied by dysmenorrhea.

The importance of x-ray applications over the region of the pituitary gland in the treatment of gynecologic disorders must also be mentioned. In 1921, L. Fraenkel<sup>116</sup> pointed out that this type of therapy could be used not only in the case of hypophyseal tumors but in patients with dysfunction of the gland as shown by disturbances in the genital organs. Geller<sup>116</sup> described an atrophy of the pelvic organs of the rabbit five months after irradiation of its head. In 1922, Hofbauer<sup>133</sup> recommended irradiation of the hypophyseal area for climacteric bleeding and hemorrhage due to fibromyomata. He later showed<sup>134</sup> that with small x-ray doses menstruation may be produced in certain amenorrheic patients, whereas larger doses in women with normal periods may result in a cessation of the menses. The problem has been taken up by a number of workers (Hirsch,<sup>135</sup> Werner,<sup>136, 137</sup> Borak,<sup>138</sup> Drips and Ford,<sup>139</sup> and others) and is now a recognized means of therapy in the treatment of functional amenorrhea, dysmenorrhea, certain forms of abnormal bleeding, etc.

#### CONCLUSIONS

It is thus seen that the existence of a definite relationship between the anterior pituitary gland and the female pelvic organs has been established. Hypophysectomy results in an atrophy of the genitalia; the administration of an extract of the anterior hypophysis produces profound changes in the ovary; the transplantation of the fresh gland stimulates the immature ovary to activity; during pregnancy and following castration there is a gross hypertrophy of the anterior lobe and an increase in the amount of the hormone in the blood and urine of the patient. A simple test for the anterior pituitary hormone, which is of

value in the diagnosis of early pregnancy, has been developed. Preliminary reports lead one to believe that an active therapeutic preparation will in time be available and the indications for its use understood. Irradiation of the hypophyseal area for certain pelvic disorders has yielded satisfactory results.

Undoubtedly a great deal yet remains obscure, but the tremendous advances of the past few years lead one to anticipate a new era in our conception of the physiology and pathology of menstruation and of the interrelationship of certain endocrine glands.

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# Selected Abstracts

## Pregnancy and Disease

Robinson: The Effect of Parturition on the Heart. *Lancet* 212: 170, 1927.

The effect of the pathologic processes, whether they be muscular, valvular, or rhythmic, is to reduce the efficiency of the heart by limiting the capacity of its reserve force. If the disease is progressive or the demand for work excessive; the reserve force is so reduced that the heart may be unable to meet the demands made upon it.

A pregnant woman with auricular fibrillation has the cardiac reserve forces depleted by the following factors: the valvular lesion, the altered rhythm, the strain of pregnancy and labor, and frequently the toxemic states in which degenerative changes are commonly found in the musculature and blood vessels.

The effect of parturition upon the normal heart is to displace it upward, with pressure on the right ventricle. The circulatory changes include plethora. The normal heart meets these demands by calling upon its reserve forces. In labor the efforts are simply those of muscular effort which always imposes a strain upon the heart and calls on the reserve. During the puerperium an additional amount of blood in the maternal circulation is present due to the contractions of the puerperal uterus which empties and occludes the vessels of the placental site.

The effect of parturition on the abnormal heart must depend upon the amount of reserve force left in the damaged organ. If this reserve is considerable, the strain may be easily overcome. If it is small the outlook is serious. If there is complete absence of reserve force or heart failure the outlook is always highly dangerous. This is supported by the fact that of the 18 patients with auricular fibrillation, which the author reports, 13 died either before, during, or soon after delivery.

The treatment of heart disease in pregnancy is summarized as follows: (1) A woman with serious depletion of the cardiac reserve forces should not become pregnant. (2) If conception occurs in the presence of seriously depleted reserves the pregnancy should be terminated before the onset of heart failure. (3) The induction of labor in the presence of heart failure is unjustifiable. (4) Artificial termination of pregnancy should be carried out when cardiac compensation has been reestablished and for many cases cesarean section is the best method of delivery.

NORMAN F. MILLER.

Oliver, Sir Thomas: Heart Disease and Pregnancy. *British M. J.* 1: 709, 1927.

The consensus of opinion is that in pregnancy there is a slight increase in the size and weight of the heart. Experiments on female dogs show that the cardiac output is increased by one-third to one-half during the later months of pregnancy. Since during the whole period of gestation there is never a fall of the arterial blood pressure, the heart is really called upon to perform a greater amount of work. Opinions differ as to whether this is accomplished by the heart becoming hypertrophied or simply by the organ calling upon its latent reserve.

Apart from myocardial failure, mitral stenosis is the cardiac lesion which gives rise to the greatest danger in pregnancy, both during and after parturition. While a cardiac patient may pass successfully through two or three pregnancies and be little worse, yet with each succeeding pregnancy the heart becomes less able to bear the strain. It dilates, and its musculature becomes less efficient. There is always a tendency toward pulmonary congestion.

With regard to the marriage of a woman with heart disease, the author considers the condition of the heart, the presence or absence of dilatation, the regularity and rapidity of the beat, the history of hemoptysis and dyspnea, as well as the social and economic status of the patient. Life is threatened mainly by changes in the myocardium and in these are included the sinoauricular node, the auriculoventricular node, and the bundle of His. The irregularities include fibrillation, extrasystoles, tachycardia, and heart-block.

If there are no symptoms the treatment consists in observation, diet, regulation of exercise, and elimination. Rest and digitalis constitute the treatment with symptoms present. If signs of fatigue or failure appear, the application of forceps is indicated in the second stage of labor. If dyspnea arises during labor, oxygen may be administered, also stimulants, such as, strychnine, etc.

ADAIR AND GRIMES.

Jensen, Fr. G.: Investigations on the Influence of Pregnancy and Parturition Upon Organic Cardiac Disease. *Acta obst. et gynec. Scandinav.* 6: 239, 1927.

The conclusions of Jensen's study are as follows:

Functional heart disease and mild cases of pregnancy toxemia are of more frequent occurrence in pregnant women who previously had rheumatic fever than in those who had previously been perfectly healthy. The character and intensity of the murmurs over the cardiac region always undergo changes in the course of pregnancy and parturition. Therefore, by means of stethoscopic examination alone it is not possible to determine whether a cardiac patient can endure the strain of pregnancy and parturition.

Pregnancy and parturition in cardiac patients are often complicated by a recurrent, toxic, endocarditis, and initial cardiac insufficiency, which symptoms, however, never set in suddenly.

In patients with mitral stenosis the power of accommodation of the myocardium, and not the narrowness of the stenosis, determines whether the patient can endure pregnancy and parturition. Therefore, one must always test the patient's response to acute exertion, simultaneously determining her blood pressure and pulse rate.

Independently of the patient's age, recurrent, toxic endocarditis occurs especially in patients with recently acquired heart disease. Endocarditis and cardiac insufficiency are indications for the interruption of pregnancy, if they do not readily yield to treatment.

Patients with heart disease are exposed to circulatory disturbances, particularly during the last four to six weeks of pregnancy. Therefore, artificial premature delivery should more frequently be resorted to than hitherto. The follow-up examination of 62 out of 119 cardiac patients showed that the prognosis of heart disease during pregnancy depends upon regular examinations of the patients from the commencement of pregnancy, and upon intensive treatment after the occurrence of the first symptoms of circulatory disturbances.

J. P. GREENHILL.

Hay, John, and Hunt, Elizabeth: A Record of Fifty Consecutive Cases of Pregnancy and Parturition in Patients with Crippled Hearts. *Lancet* 224: 271, 1928.

An added strain in pregnancy occurs with the increased weight, the enlargement of the uterus and breasts, and the dilated vessels; and in the last third of pregnancy, with interference of the diaphragm, displacement of the heart, and chest changes. The effects are more noticeable in primigravidae, and the discomforts and difficulties increase with the advance of pregnancy.



The first stage of labor does not put a severe strain on the heart, even with exhaustion, but the second stage is the important phase. Because of the drop in the blood pressure, the patient may collapse or may have a severe hemorrhage immediately after delivery.

With auricular fibrillation the author does not induce labor until specific treatment with digitalis has failed. Generally, induction of labor is advisable over cesarean section in any of the cardiac complications.

Rest and sedatives are valuable in the first stage, and instrumental help early in the second stage. During pregnancy rest with "specific treatment" is recommended.

The writer is not strictly opposed to pregnancies in cardiac patients, although there is an increased danger to the mother. The heart usually responds very well to treatment during gestation.

II. C. HESSELTINE.

Sachs, E.: Management of Labor in the Patient with Cardiac Disease. *Deutsche med. Wehnschr.* 54: 45, 1928.

The most important problem is the treatment of the diseased heart. Interruption of pregnancy is the last thing to be considered, even in early pregnancies. If rest and proper medication does not restore the disturbed compensation then termination of pregnancy certainly will not prove beneficial.

The situation is different in advanced pregnancy because there are mechanical conditions and special demands on heart action, etc., which might add to the existing difficulties, but even under these conditions the restoration of compensation is the prime task of all therapy.

The value of proper psychic influence should not be undervalued. The patient must be assured that her physician will be with her during labor, that all unnecessary pain and physical effort will be avoided as far as possible.

Inability to combat decompensation and extracardial complications (nephritis) render prognosis bad. It is necessary to avoid all sudden fluctuations in blood pressure, incident to emotions, bearing down efforts, escape of blood into abdominal viscera after expulsion of the fetus, etc.

Earlier in labor, the quinine—ether—oil enema works satisfactorily, later to be supplanted with twilight. The labor is terminated quicker by use of a pituitary preparation, forceps, or extraction in breech presentation. Prompt administration of ergot and application of a heavy sandbag on the abdomen, immediately after expulsion of baby, prevents sudden fall in blood pressure and "empty pumping" of heart as result of large quantities of blood passing into the visceral blood vessels. Puerperium itself, if normal, holds no further dangers. These patients always should be managed in hospitals.

Cesarean section the writer reserves only for cases with added complications such as narrow pelvis, placenta previa or prolapsed cord because in the cesarean operation the sudden fall in blood pressure can be combated solely with ergot. The operation is preferably done under lumbar anesthesia, but it is his belief, that delivery through the vagina is safer than cesarean for all cardiac patients.

GRUENFELD.

Zinsstag, G.: Pregnancy and Mitral Stenosis. *Monatschr. f. Geburtsh. u. Gynäk.* 75: 498, 1927.

The author reports three fatal cases of mitral stenosis which occurred in pregnant women. He is convinced that contrary to some opinions, mitral stenosis can be a very serious complication in pregnancy. In these cases, signs of decompensation which are usually present with other forms of heart trouble, are frequently

entirely absent. In many instances death occurs suddenly in an apparently healthy woman. Statistics are of very little significance. In the Aarau and also in the Basle clinics, all the fatal cases of heart disease during pregnancy were in women who had mitral stenosis. The author believes that pregnancy should be interrupted in cases of mitral stenosis regardless of whether or not signs of decompensation are present. Exceptions may be made in primiparas but there is danger in them also. Cesarean section under local anesthesia is a very commendable form of delivery and should be used frequently. Sterilization should always be performed.

J. P. GREENHILL.

von Jaschke: Pregnancy and Mitralstenosis. *Zentralbl. f. Gynäk.* 51: 1350, 1927.

Contrary to the opinion of many German obstetricians, von Jaschke does not approve of interruption of pregnancy, when complicated by a well compensated mitral stenosis. This lesion is likely to become decompensated but only then abortion is to be performed. Lumbar anesthesia is preferable to any form of inhalation anesthesia. Cases, reported by others to have taken a disastrous course during or after pregnancy, were all complicated by pericarditis, myocarditis, etc.

GROVER LIESE.

Mahon, R.: Hereditary Tuberculosis. *Rev. franç. de gynéc. et d'obst.* 22: 193, 1927.

Modern literature seems to show that hereditary tuberculosis does not exist. Undoubtedly a woman with advanced tuberculosis often gives birth to a nonviable fetus. However in these instances the tuberculosis acts like any general illness which causes premature labor but it is not a specific action. There are two aspects in the heredity of defective ova. The first is the transplacental contamination with the tubercle bacillus but this is rare. The second is the transplacental transmission with the filterable form of the tuberculous virus but this is still rarer than the first. Clinical research has definitely shown that the very large majority of children born of tuberculous parents remain well and grow up healthy. If infants cannot be protected against tuberculous infection they should be immunized by the injection of Calmette and Guérin's vaccine.

J. P. GREENHILL.

Hill, Allis M.: A Statistical Study of the relationship Between Pregnancy and Tuberculosis. *Am. Rev. Tuberc.* 17: 113, 1928.

This study includes 349 women whose pregnancies occurred during, or immediately preceded, pulmonary disease, and of 160 women as controls who had been pregnant but whose condition was not tuberculous. Comparison of these two groups leads the author to conclude that pregnancy had no appreciable bearing upon the progress of the pulmonary condition. The earlier the diagnosis was made the less hazardous were their pregnancies. The highest mortality occurred among primiparae. Primiparae constituted 15 per cent of the women diagnosed before pregnancy, 21 per cent during and 32 per cent after confinement. The maternal mortality for tuberculous women corresponded to the mortality rate among registered females of the same ages. As to sanatorium treatment, only one-third of the 349 patients had as much as six weeks of institutional care, and many more were hospitalized after delivery than diagnosed before or during pregnancy.

In an attempt to obtain more data concerning the relationship of tuberculosis to pregnancy, the author urges the use of a uniform scheme or history which should be sent, properly filled out, to the National Tuberculosis Association at the close of the case.

SIGOLOFF.

Bridgman, E. W.: Pulmonary Tuberculosis and Pregnancy. *Bull. Johns Hopkins Hosp.* 38: 83, 1926.

This study is based on 14,000 records of indoor obstetric cases admitted to the Johns Hopkins Hospital. Of these, 134 had evidence of pulmonary tuberculosis in some form. There was about an equal number of whites and blacks, with a large percentage of multiparae. The 134 patients were grouped as follows: (1) questionable tuberculosis; (2) definite but inactive pulmonary tuberculosis; (3) definite active tuberculosis of the lungs upon whom therapeutic abortion was not performed; (4) definite tuberculosis of the lungs upon whom therapeutic abortion was induced, and (5) pulmonary tuberculosis associated with other diseases.

Where there is a far advanced or an acute, rapidly spreading tuberculosis, pregnancy serves as the final straw and practically assures a lethal outcome. The author feels that pregnancy should be avoided in the presence of an active tuberculosis as in the series it proved disastrous. Operative treatment, however, in the presence of an active tuberculosis is followed by a higher mortality rate than the expectant treatment. Artificial termination of pregnancy is not indicated in a pregnant woman with an active tuberculosis. Treat the tuberculosis to the uttermost, but disregard the pregnancy. The tuberculous mother should not be subjected to repeated pregnancies. Tubal sterilization should be resorted to in appropriate cases after consultation between obstetrician and practitioner. Lactation should be avoided or limited because of the harmful effect on the mother and danger of infecting the baby. Statistics from their own cases and from those of others indicate that 50 per cent of the infants born to mothers with an active tuberculosis die within the first year of their lives.

ADAIR.

Jeannin, M.: Concerning the Influence of Pregnancy on Pulmonary Tuberculosis. *Le Progres méd.* No. 28, 1083, 1927.

Pregnancy is incapable of exercising a favorable influence upon the focus, even granted that occasionally the condition of the lesions remains stationary, as might be the case in the sclerous and extremely resistant forms. Pregnancy in the great majority of cases seriously aggravates the tuberculosis, especially where the infection makes its appearance during a pregnancy. The worst effect seems to be in the early months, the latter months, and especially immediately after delivery. A very harmful rôle can be assigned to repeated pregnancies, especially if coming close together. The wide extension of the infection during pregnancy, and also frequent involvement of the larynx, is pointed out. Lactation, toxemic vomiting, etc., all exert a harmful effect. The proved fact of generalized lowered resistance during pregnancy is given as an additional explanation of its unfavorable effect on the tuberculosis.

Medical treatment should be scrupulous. Artificial pneumothorax may be advisable. From the obstetric standpoint interruption of the pregnancy is essential but should not be done after the third or at most the fourth month. The results of interruption of pregnancy appear to the author very good. Either a curettage or hysterectomy should be performed, the latter being the operation of choice, where the question of sterilizing the patient arises.

SCHAUFFLER.

Goldschmidt, H.: The Fate of Women After Postponed Interruption of Pregnancy. *Med. Klin.* 24: 1003, 1928.

The author followed up 14 patients who had serious medical ailments during pregnancy but for which the pregnancy was not interrupted. Eight patients had pulmonary tuberculosis, three had cardiac decompensation, one had bronchial asthma

and two had general asthenia. Not one of the eight tuberculous patients died but all lost weight after delivery. Two patients had to continue treatment for their pulmonary condition. Seven of the patients went to full term and one had an abortion. All the deliveries were uncomplicated. Of the eight babies (one pair of twins), two died during the first year of life. The author also followed up ten tuberculous women in whom pregnancy had been interrupted for the pulmonary condition and he found that three died within two years of the operation. Of the three patients with cardiac decompensation who were permitted to continue their pregnancy, two were well but one had many cardiac complications.

J. P. GREENHILL.

**Couvellaire, A.: The Newborn Child of the Tuberculous Mother.** *Presse médicale* 15: 225-227, 1927.

Since 1921, a special maternity pavilion for tuberculous mothers at the Baude-locque clinic has cared for 356 pregnant mothers; 357 fetuses or full-term children have been born. No therapeutic abortions have been performed, as Couvellaire does not feel that definite benefit can thereby be assured the mother. Three hundred and nineteen children were born living and apparently susceptible of being reared, though half of them had a birth weight of 3000 grams or less. These children were immediately separated from their mothers and were cared for in a special department, with all provisions against postnatal maternal contagion. Of these, 56 died during the first thirty days after birth; this loss is larger than that noted in general statistics of neonatal mortality. There has been a steady decline in the mortality rate. This improvement is ascribed to the isolation of and expert care for the babies, and to the use of human milk.

This mortality has been studied from two points of view: (1) the course of the disease in the mother during pregnancy, whether active, or of slow, chronic evolution; (2) the possibility of the placental transmission of the tuberculous virus.

Under the first heading he found that the initial loss (pregnancy, birth, and first three days of life) was 14 out of 41 for the active group, and 5 out of 85 for the second, or chronic, group. The higher fetal mortality of the first group is due to the larger number of spontaneous interruptions of pregnancy before term, under the influence of the maternal infection.

Under the second heading are noted some autopsy and experimental findings. Eight fetuses born dead or dying shortly after birth were autopsied, and guinea pigs were inoculated with suspensions and filtrates prepared from various organs and tissues. In two instances, both the autopsy and inoculation results were entirely negative. In 3 fetuses (2 of them from mothers dying of tuberculous meningitis), bacilli without demonstrable tuberculous lesions were found at autopsy in coronary and mesenteric lymph nodes and at the hilum of the liver. In 6 instances, guinea pig inoculation with tissue juices produced in some of the animals a few bacillary forms in scattered groups of lymph nodes. In two of these cases (one from a case of tuberculous meningitis in the mother), guinea pig inoculation with filtrates was followed by the development of acid-fast organisms in some lymph nodes. None of the guinea pigs presented the anatomic lesions of tuberculosis.

The author has noted that some children of tuberculous mothers, which were apparently normal at birth, have developed a "progressive denutrition" leading slowly to death. Autopsy of two of these infants disclosed no lesions of tuberculosis, but guinea pig inoculation resulted in a few scattered acid-fast bacilli. Such children are carriers of a tuberculous-virus which has been transmitted through the placenta, and in the early weeks of life leaves no discernible lesion. He has never seen a frank case of congenital tuberculosis, with lesions developed in utero.

The writer concludes that the mortality rate of these children during the first weeks of life is primarily determined by care and surroundings, and that under proper conditions, with protection from postnatal maternal infection, they can as a rule be reared as successfully as the children of healthy mothers cared for under similar conditions.

E. L. KING.

Fraymann, S.: Toxic and Mechanical Causes of Visual Disturbances During Pregnancy and Labor. *Monatschr. f. Geburtsh. u. Gynäk.* 76: 216, 1927.

Amaurosis can be the first manifestation of a severe toxemia. The author reports the only case on record of homonymous hemianopia during labor associated with eclampsia. The homonymous hemianopia in this case was due either to true hypertrophy of the hypophysis with an asymmetric sella turcica or to unilateral hemorrhage in the hypophysis accompanied by pressure on the right optic tract. Pregnancy should be terminated not only when toxic amaurosis is present but also when there is hemianopia. The author urges that more attention be paid to examinations of the eyes during pregnancy.

J. P. GREENHILL.

Springer, A.: Diabetes and Pregnancy. *Wien. klin. Wchnschr.* 38: 1108, 1925.

The author describes in detail two cases of pregnancy and labor in diabetic mothers in which the babies weighed 5250 and 7000 gm. respectively and draws attention to the fact that, although diabetics are as a rule sterile, when they conceive and carry to term, the fetus is usually of gigantic size. He agrees with Folliet that this gigantism is probably due to the maternal hyperglycemia. He cannot, however, explain the fact that 50 per cent of pregnancies in diabetic women terminate in early miscarriage or in premature labor.

RALPH A. REIS.

Faber, Knud: The Threshold of the Blood Sugar in the Glycosurias of Diabetics and of Pregnant Women. *La Presse Médicale*, p. 1109, Sept. 10, 1927.

The sugar threshold is constant for a given individual, diabetic or not, but it may vary notably in different individuals. In most diabetics the level is found between 150 and 230 mg. per 100 c.c. of blood. It is found between the same levels in some individuals having a normal carbohydrate metabolism without glycosuria, but in many such individuals it is lower. However, if the blood sugar level is between 100 and 150, a "cyclic alimentary glycosuria" is often found; if the level is lower, the elimination of sugar may be almost constant, the so-called renal glycosuria. A person with a very low threshold may be afflicted with a "diabetic anomaly of metabolism"; in this case the glycosuria is very hard to overcome, on account of the very low level at which the blood sugar must be kept.

The threshold of a given person may be modified under the influence of certain conditions; e.g., phloridzin glycosuria and the glycosuria of pregnancy. The latter often occurs in association with a normal glycemia, and the development of alimentary glycosuria has recently been advocated as a test of pregnancy; however, it is not sufficiently reliable to be of value.

The author decided to determine if the glycosuria of pregnancy is due exclusively to a lowering of the threshold, and if this is purely a temporary phenomenon. In two primiparae, both showing glycosuria during the day but free from it in the morning, he found the blood sugar levels before delivery to be between 95 and 131. Eight days after delivery it was 156 and 142, respectively. Two and seven months after delivery, respectively, the figures were 150 and 197, without

glycosuria. In the first patient, he also employed the alimentary glycosuria test before and after delivery, making blood sugar determinations and urinalyses every two to five minutes. He found that during pregnancy, after the administration of 25 gm. of glucose, glycosuria developed at the maximum figure of 132, and persisted until it fell to 52. After 15 gm. of glucose, no glycosuria developed. Eight hours after delivery, following the administration of 25 gm. of glucose, the blood sugar rose to 156 without glycosuria; however, 40 minutes after the maximum rise of the blood sugar a pronounced glycosuria was found. Six months later, after the administration of 100 gm. of glucose, the blood sugar rose to 197, without glycosuria.

The low blood sugar level of a fasting pregnant woman is especially to be noted, as well as the disappearance of the hypoglycemia after delivery.

E. L. KING.

**Marsalek, Jan M.: A Case of Sudden Death During Pregnancy.** Bratisl. lekar. listy. 7: 529, 1927.

A primipara, twenty-three years old, was admitted in deep coma. She was well developed, had previously been in good health. Her respirations were regular, deep and sonorous. A history was obtained, which stated that twelve hours previously she became dizzy and nauseated. She had frequent attacks of vomiting. She answered questions incoherently and seemed confused, then had several convulsions in rapid succession.

Examination showed head deviated to the left, face flushed, pulse 76, systolic pressure 120, râles in base of both lungs.

Uterus is four fingers below the xiphoid process, fetal position O. D. A.

The patellar reflexes were exaggerated, with a positive Babinski and Oppenheim sign on the right, and more marked on the left side. Ankle and patellar clonus could not be elicited.

Catheterized specimen contained no albumin, but considerable amount of sugar. Exitus occurred suddenly, three hours later.

At autopsy, a tumor, the size of a child's fist was found in the left cerebral hemisphere, which proved to be a very vascular gliosarcoma.

JOHN SOUKUP.

**McIlroy, Louise A.: The Influence of Parturition Upon Insanity and Crime.** The Lancet 214: 379, 1928.

In this medicolegal article the writer states that puerperal insanity accounts for 10 per cent of female lunacy, and in this group suicide and infanticide not infrequently occur. The crime may be committed in the puerperal period or during lactation.

The three chief forms of puerperal insanity are confusional, intermittent (manic-depressive) and dementia precox. Strains, exhaustion, infection, labor, or lactation may precipitate the mental state. The prognosis is poor in dementia precox. Not infrequently it may recur in following pregnancies and puerperiums.

The writer makes a plea for an adjustment and definition of the laws in England to prevent permanently branding the temporarily insane mothers for their rash acts, and yet to provide exacting punishment for sane infanticide crimes.

H. C. HESSELTINE.

**Waldstein, E.: Status Epilepticus and Pregnancy.** Monatschr. f. Geburtsh. u. Gynäk. 78: 164, 1928.

The author reviews the literature on the association of epilepsy and pregnancy and describes a case of his own. In this case clinical studies as well as autopsy

definitely excluded eclampsia, the only case on record where the child remained alive. A cesarean section was done and the patient had no convulsions for thirty hours after the operation. Then she had convulsions which occurred at five to fifteen minute intervals until she died. In an interval of two and a half days she had 180 convulsions. Autopsy revealed as cause, six calcified cysticercuses situated over both cortexes and under the right frontal lobe. Among the 23 epileptic patients whose histories were reported there were 54 pregnancies. Forty gestations went to term, five ended prematurely and ten ended early as abortions. Hence it appears that epilepsy itself does not disturb pregnancy and, therefore, is no indication for therapeutic interruption of pregnancy. Gestation seldom makes epilepsy worse. In fact in half the cases an improvement was observed. Cesarean section is the best method of delivery.

J. P. GREENHILL.

Eufinger, H.: A Case of Transitory Delirium During Labor. Med. Klin. 22: 1107, 1926.

The psychic and somatic condition of a pregnant woman often borders on the pathologic and it is astonishing that mental disturbances do not occur more frequently during labor. Gestational psychoses have been reported quite often but there are few reported instances of transitory insanity during labor. In the latter cases, the immediate cause is the somatic and psychic trauma of labor but there must exist a psychopathic tendency. The author reports a case of temporary insanity during labor in a thirty-eight-year-old primipara. The family and past history of the patient revealed no abnormalities. After a forty hour labor and slow progress the patient was brought to the hospital. On admission she showed marked restlessness, disorientation and drowsiness. An attempt was made to hasten labor by means of a colpeurynter but the patient pulled the bag out of the uterus. After an unsuccessful attempt to deliver the child with forceps, a craniotomy was performed. Immediately after this, the patient became completely orientated. The patient's physician after delivery, said he had given the patient a hypodermic of scopolamine (0.3 mg.) before admission. In this case the delirium lasted one and one-half days.

J. P. GREENHILL.

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## Correspondence

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### The Classification of the Toxemias of Pregnancy

*To the Editor.*—Due to an error in transcribing notes a mistake occurred in my article in the July number of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY. On page 41, line 11, the phrase "edema universal in extent" should have read "absence of edema."

PHILIP F. WILLIAMS, M.D.

2206 LOCUST ST., PHILADELPHIA, PA.

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## Original Communications

### FURTHER OBSERVATIONS ON THE HEPATIC LESION IN ECLAMPSIA\*

BY WILLIAM J. DIECKMANN, B.S., M.D., ST. LOUIS, MISSOURI

*(From the Department of Obstetrics and Gynecology, Washington University School  
of Medicine and the Saint Louis Maternity Hospital)*

IN CONSIDERING various factors which may be involved in the production of the clinical condition which we designate eclampsia, our attention has been focused on the lesion which is found in the liver of many patients dying of this disease. This lesion is chiefly a peripheral hemorrhage associated with necrosis and a process which has not been demonstrated in any other condition but in eclampsia. It is pointed out clearly in the literature that these changes are not necessarily present in the liver in every case but most reports show that they are present in a very considerable majority of cases. We do not wish to create the impression that the hepatic lesion is the most important phase of clinical eclampsia but rather that it is a specific one and its importance in the disease can only be expressed after other phases of eclampsia are better explained.

Fahr summarizes the changes in the liver in eclampsia briefly as follows: Localized changes are found in the periphery of the lobule and fibrin thrombi in the portal capillaries. This condition in the capillaries leads to the production of large blood spaces and hemorrhages which bring about necrosis of the liver tissue involved, chiefly by pressure. In view of this fact and also of the fact that in eclampsia thrombosis in other parts of the body is not nearly so frequent as it is in the liver, conditions must exist there which favor coagulation in the portal capillaries.

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\*Read at a meeting of the New York Obstetrical Society, May 14, 1929.

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NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."



In a previous paper we have discussed possible ways in which this coagulation might take place. In the first place portions of placental tissue are constantly entering the maternal blood stream. This is more marked in the latter weeks of pregnancy at the time eclampsia is most likely to develop. This tissue, being whole protein and, as we have demonstrated, high in tissue fibrinogen, might not only cause some shortening of the coagulation time but also might be considered a factor in producing the increased fibrinogen content of the blood occurring in late pregnancy and more particularly in eclampsia. To bring about neutralization or digestion of these elements which are continually entering the blood stream a certain amount of neutralizing substances

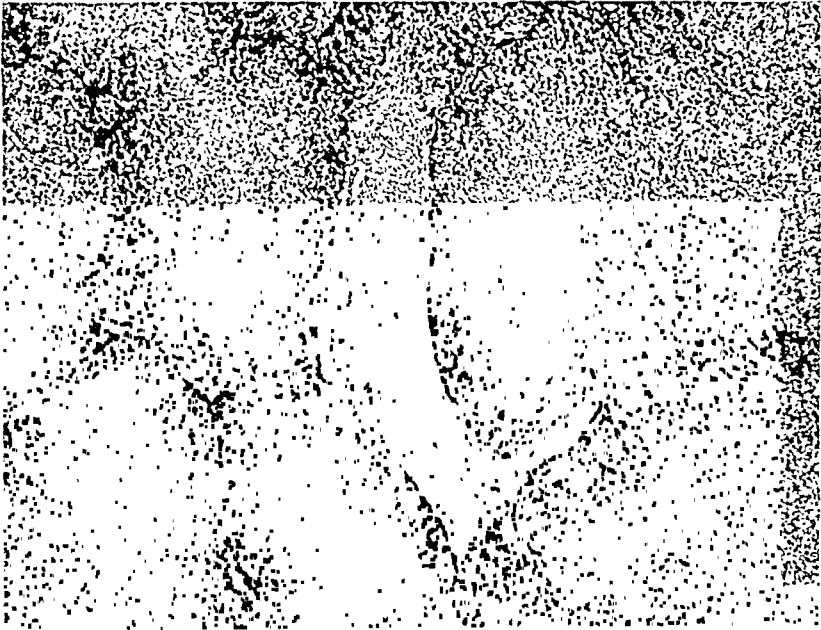


Fig. 1.—Dog 67. In the center of the picture is seen a portal space entirely surrounded by hemorrhage and beginning necrosis. This lesion was very extensive and one meat protein meal and one injection of tissue fibrinogen (lung extract) caused the death of the dog in convulsions four hours later.

or ferments of the blood must be called upon to do this work. Further it has been shown by Mills, whose work I quoted in detail in a previous paper, that so-called tissue fibrinogen when given by mouth has a marked effect on shortening the coagulation time and can even be demonstrated unchanged in the urine. Mills has also shown that there is in the human a marked shortening of coagulation time following the ingestion of a meal rich in meat protein. This work of Mills suggested to us that in pregnancy there is perhaps an increased permeability of the intestinal wall just as there is increased permeability in other tissues of the body during this time. Under these conditions larger protein molecules than the amino-acid derivatives could be absorbed and become concentrated in the portal circulation. This point interested us further when

we recalled the fact that if certain precautions were taken in the latter months of pregnancy, eclampsia seldom develops. These precautions consist of the elimination of meat proteins from the diet, effective daily evacuations of the bowels, and the intake of a considerable amount of fluid.

When one considers the high blood pressure which is practically always present in cases of eclampsia and recalls the marked changes in the capillary circulation which have been observed by numerous investigators, it is logical to assume that some pressor substance or substances are at work. What the nature and source of this substance or substances may be has been a point of much discussion and considerable

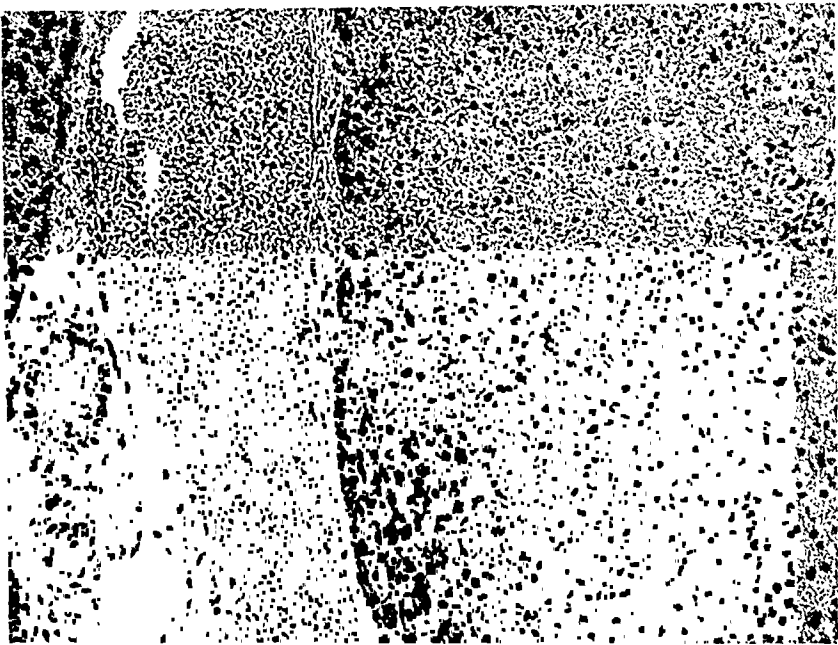


Fig. 2.—Dog 67. Higher power of Fig. 1. Shows branch of portal vein and bile duct. Just a small strand of normal liver cells remains to right of vein.

investigation. It is logical to assume that no one source is responsible for the presence of such substances. That the intestinal tract may be a source is a logical deduction from the fact that in intestinal putrefaction amines are formed which if absorbed could act as pressor substances. This may be a group of amines and not any particular isolated one. The placenta could be regarded as another source, the degenerative lesions there could be considered as well as the normal structures which enter the blood stream almost constantly. A damaged liver may also be considered as a source which may result directly in releasing additional pressor substances and also may lead to a diminution of the formation of antithrombin thereby further shortening coagulation. Probably all these sources and under rarer circumstances even others could be considered; in the one case, one may be the most predominant

factor, and in another case, another. Our attention has been called recently to the work of Johnson, Johnston and Nichols. These investigators feel that an increased tyramin content of the blood may be a factor in the production of eclampsia. From their conclusion they emphasize the placenta as the chief source of this material. As we have stated we have long been aware of the fact that substances of this kind may be at work in eclampsia, but we repeat that these substances are most likely not from any specific substance or from one particular source. With a concentration of blood resulting from the action of such pressor substances, the increased concentration of the products in the portal system due to the absorption from the intestinal tract, and with the usual neutralizing substances working against the ever-entering

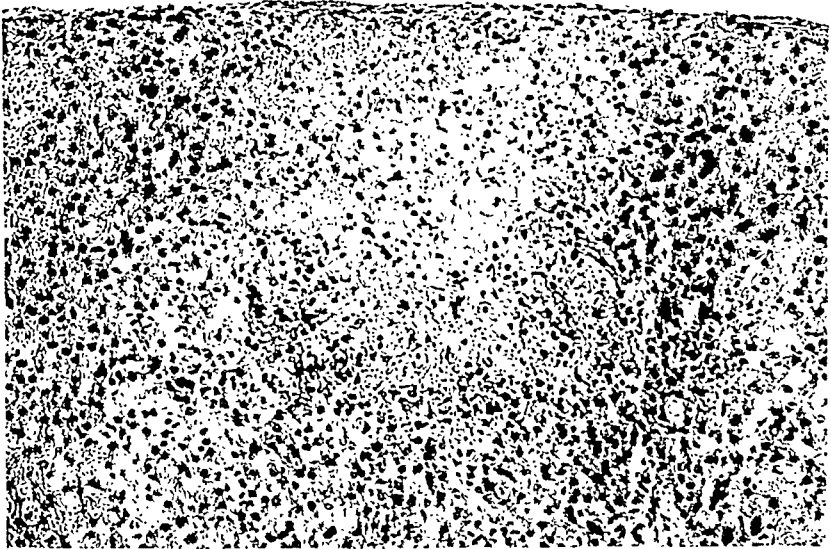


Fig. 3.—Dog 67. Periphery of liver, showing marked subcapsular hemorrhage with beginning necrosis.

placental elements in the blood, we can conceive that a very likely place for coagulation to occur under such conditions would be in the small tributaries in the portal vein in the liver.

From these deductions we attempted to produce experimentally in the dog conditions similar to two of these factors. First, the entering of placental elements in the blood stream. This tissue has a high fibrinogen content and we felt that by the injection of tissue fibrinogen into the general circulation this could perhaps be considered analogous. Second, the injection directly into the portal vein of the same substance after the injection into the general circulation would give a higher concentration of tissue fibrinogen there. We did this in a small series of experiments and were able to show very clearly that marked hemorrhage and necrosis in the periphery of the lobule could be produced as

well as marked portal thrombosis. We then resorted to the injection of tissue fibrinogen in the general circulation and in addition gave it by mouth. In this way we were able to produce lesions similar to those occurring in the first series but not quite so extensive. This work has been reported in two previous publications.

Somewhat encouraged by these results we felt that if the observations of Mills concerning the ingestion of meat protein on the coagulation time was correct we should be able, by continuing the injections in the general circulation and by giving full meals of raw meat by mouth, to produce a coagulation in the tributaries of the portal system in the liver which should produce hemorrhages and necrosis. Our results in this series are the basis of this report.

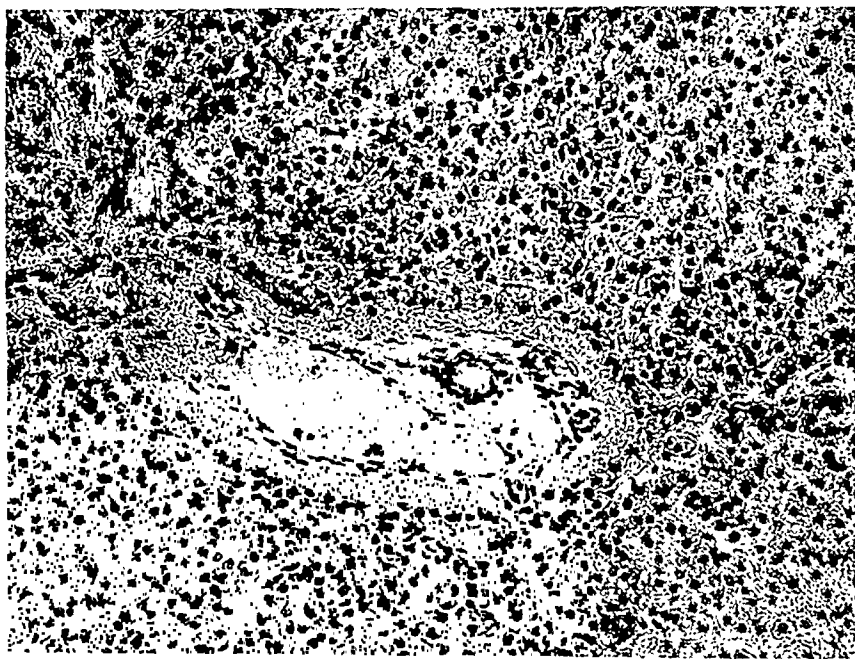


Fig. 4.—Dog 55. A small portal space with marked distention of vein around the periphery; smaller vessels leading to this are likewise distended. Very little hemorrhage observed elsewhere in liver, but in numerous places hemorrhage is seen in the periphery of the lobule, some quite extensive. (See Fig. 5.)

A series of 43 dogs were studied. The dogs received a full meal of raw meat daily followed by the injection of tissue fibrinogen or lung extract in the general circulation one hour later; the dosage varied from  $\frac{1}{2}$  to 3 c.c. of tissue fibrinogen or lung extract. Frequently after the injection in the general circulation the animal would cry out, urinate, have evacuations from the bowels, and develop convulsions. The animals were sacrificed at various periods from two to seven days; they were always sacrificed when the symptoms produced by the injections were marked, so as not to have the animal die during the night. In this series of 43 dogs, 22 cases were selected as showing definite lesions. These lesions were described as hemorrhages under the capsule of the

liver and in the periphery of the lobule in that region with necrosis, as midzonal and necrosis, as peripheral hemorrhages and necrosis, and as

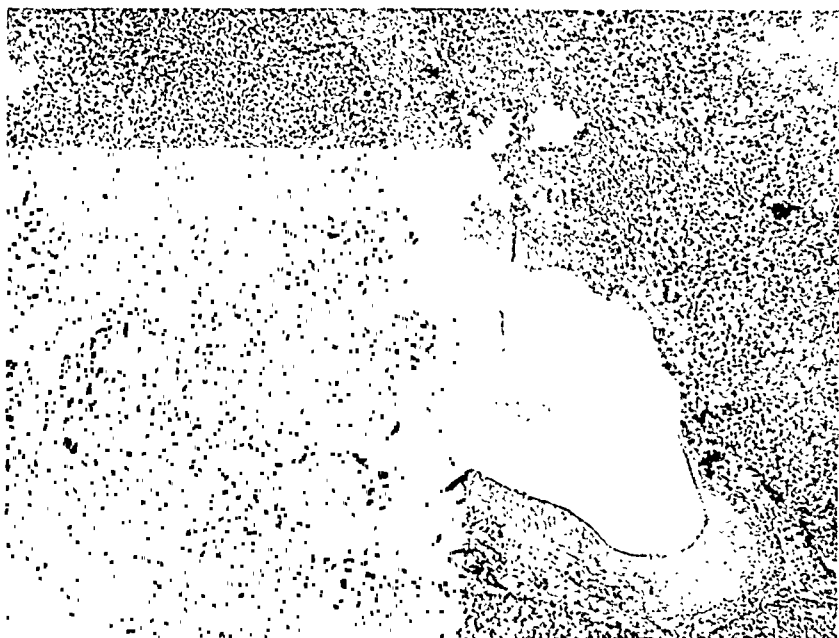


Fig. 5.—Dog 55. Larger portal space. Large dilated portal vein entirely surrounded by an area of hemorrhage. A marked area of hemorrhage and necrosis about 2 cm. in diameter above it. Tissue very friable here and tore easily in handling sections. Bile duct and artery below and to left of vein.

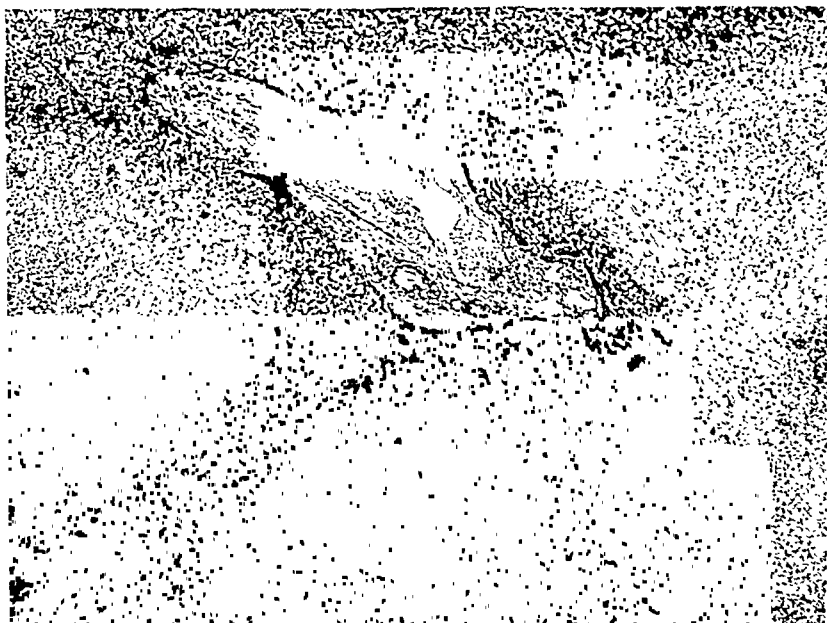


Fig. 6.—Dog. 36. Very extensive hemorrhage and marked necrosis similar to Fig. 1 in distribution but necrosis more marked. Lesion produced in nine days.

portal vein thrombosis. Only organizing thrombi in the larger branches of the portal vein in the liver were considered as evidence of thrombosis.

The most marked lesions present were the hemorrhages in the periphery of the lobule underneath the capsule frequently associated with marked necrosis. Almost equally striking were the marked midzonal hemor-

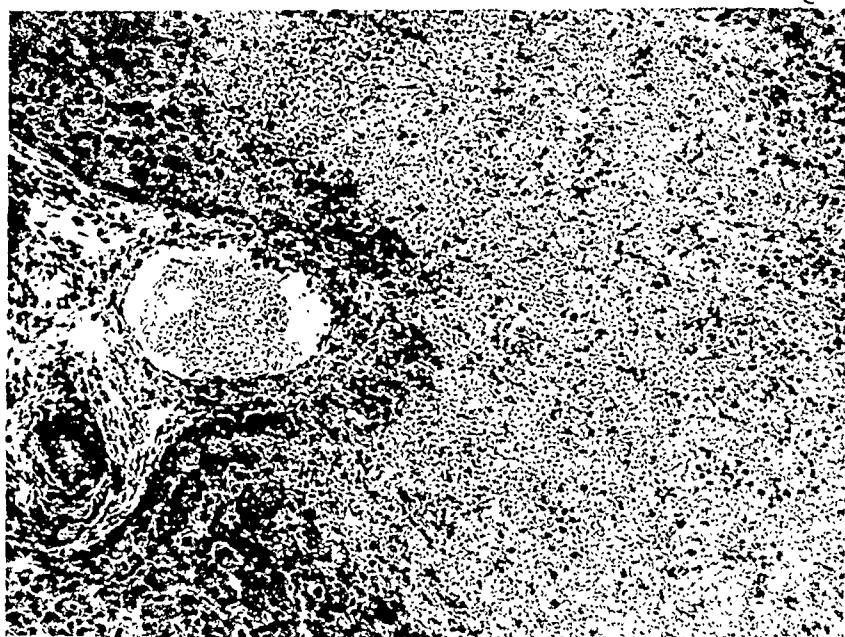


Fig. 7.—Dog. 36. Higher power, showing the marked necrosis and the lesions extending into the portal space.



Fig. 8.—Dog 64. Marked hemorrhage and necrosis, chiefly midzonal, but so extensive that practically the entire field is involved. Very small amount of normal liver tissue remains around portal space to left of center.

rhages with marked areas of necrosis and least striking were the peripheral hemorrhages and necrosis about the portal spaces. Marked

TABLE I

SERIES NO.	DOG NO.	GROSS LESION	SUBCAPSULAR		MIDZONAL		PERIPHERAL		PORTAL VEIN THROMBOSIS
			HEM.	NEC.	HEM.	NEC.	HEM.	NEC.	
1	31	Marked Mottling Rt.	2	2	2	1	2	1	--
2	33	Mottling Rt.	3	1	3	1	2	2	--
3	36	Hemorrhage, Extensive Rt.	3	3	3	3	3	3	1
4	39	Mottling	2	--	2	1	--	--	3
5	40	-----	2	2	2	2	2	2	--
6	41	Hemorrhage, Mottling	2	1	2	1	2	--	3
7	42	-----	3	3	2	2	2	1	3
8	43	Hemorrhage Rt.	2	1	2	2	2	1	3
9	55	Mottling	2	1	2	2	2	2	3
10	56	-----	1	--	1	--	1	--	3
11	58	Speckled	3	3	2	1	1	1	3
12	60	Speckled	1	--	1	--	1	--	3
13	61	Hemorrhage Rt.	2	2	2	1	1	1	--
14	62	Hemorrhage Rt.	3	2	3	1	--	--	--
15	63	Hemorrhage, Extensive Rt.	2	2	2	2	1	--	3
16	64	Hemorrhage Rt.	3	3	3	3	3	3	1
17	67	Marked Mottling Rt.	3	3	3	3	3	3	--
18	69	Hemorrhage Rt.	3	2	2	2	--	--	3
19	71	Speckled	2	2	1	1	1	--	3
20	73	Hemorrhage Rt.	3	3	3	1	1	--	--
21	74	-----	3	3	3	3	1	--	--
22	79	Hemorrhage, Extensive	3	1	3	1	--	--	--

NOTE: 1, Moderate lesion. 2, Marked lesion. 3, Very marked. Hem., Hemorrhage. Nec., Necrosis. Rt., Right side of liver.

portal thrombosis was found in quite a number of cases. Table I will show the location and extent of these lesions. In the gross many of

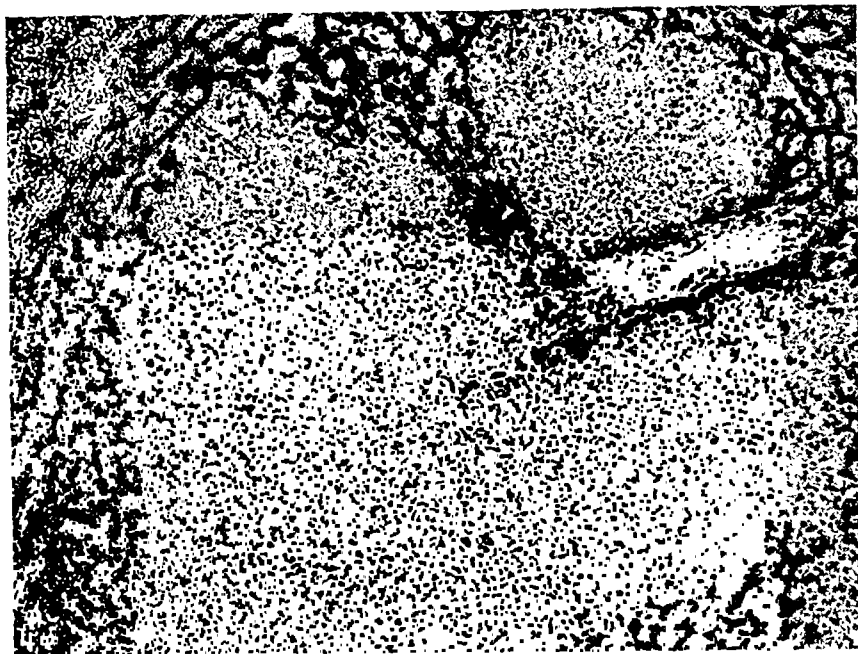


Fig. 9.—Dog 69. Marked midzonal hemorrhage and necrosis.

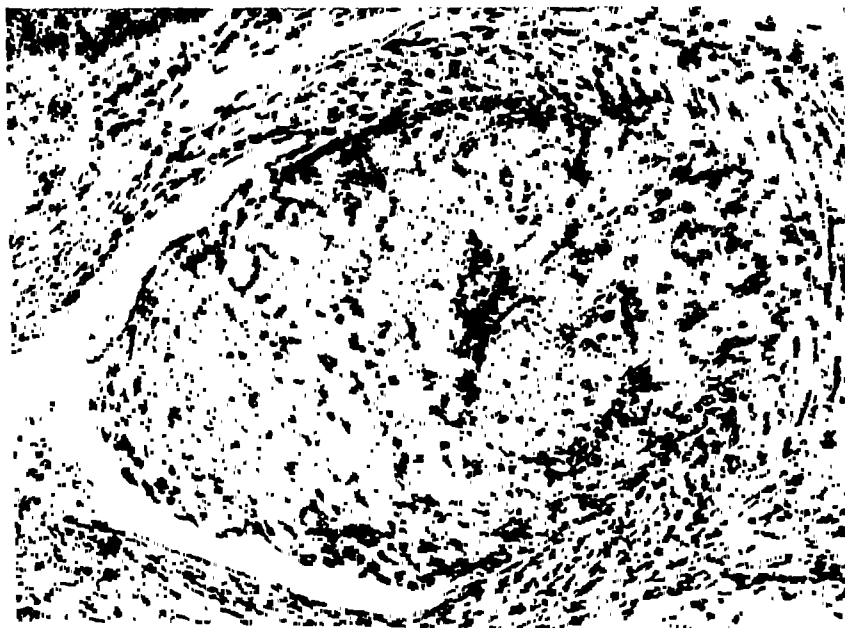


Fig. 10.—Dog 69. Organized thrombus in larger branch of portal vein. Neighboring bile duct and branch of hepatic artery not seen in picture.

the specimens showed hemorrhage in the liver of considerable size with a certain degree of small mottling due to smaller hemorrhages.

The chief difference in this series from our first report was the



production of a marked midzonal hemorrhage with necrosis. These lesions in their appearance were entirely similar to the lesion in eclampsia except that the midzonal area was the origin of the hemorrhage. The hemorrhage extended most markedly from this area to the periphery of the lobule and one might be deceived in regarding the lesion as peripheral. This definitely was not the case. We were at a loss to explain why this should occur but felt that it was possible that coagulation began in the tributaries of the portal vein near the midzonal area and these blood spaces would burst before coagulation could take place in their continuations toward the periphery of the lobule. Under such conditions the blood could escape in the midzonal area first. We felt, however, that the mechanism of the production of this hemorrhage was similar whether it occurred midzonally or peripherally, as the lesion in both locations was essentially a hemorrhage followed by a necrosis in the involved area.

In some cases there was extensive portal thrombosis, recognized by finding marked organized thrombi in larger branches of the portal vein within the liver. Wherever such thrombosis is designated in the chart, organization had taken place in these thrombi. In practically all cases the tributaries of the portal vein were markedly overloaded with blood, many showing marked agglutination of red cells with beginning thrombus formation. We did not include these as evidence of thrombosis unless organization was already present. This was true also in many of the negative cases in which there was a considerable amount of hemorrhage in the periphery of the lobule under the liver capsule. These lesions, however, were regarded as insignificant and therefore disregarded. From our experience with this series, we realize from the reaction in the individual dog and the varying character of the lesions produced that our methods are still comparatively crude and further experience is needed. We are now beginning a series in which smaller doses will be used over a longer period of time accompanied by a pressor substance such as tyramine in order to imitate the action of such substances supposedly present in human eclampsia.

#### SUMMARY

Although the lesion which has been produced in this series is not typically that of eclampsia, we feel that it is due to the coagulation of red blood cells in the portal vessels of the midzonal area with hemorrhage beginning at this point and a necrosis resulting in the involved tissue. In other words, the same mechanism produces this lesion which is apparently at work in the production of the lesion of eclampsia in the human. As a result of marked hemorrhage and necrosis as well as portal thrombosis produced in some of these cases, we think that substances which were absorbed from the intestinal tract and concentrated in the portal system overloaded this system under the conditions

of the general circulatory injection of tissue fibrinogen and was an added factor in bringing about coagulation in the portal system within the liver.

We feel that the idea of Mills that a marked shortening of coagulation time after the ingestion of a meal rich in meat protein is substantiated by these experiments. One of the striking features of lesions in this series was the rapidity with which extensive damage occurred in some of the cases. This is particularly well shown in Case 67, which is illustrated (Figs. 1, 2 and 3). This dog received 1 c.c. of lung extract one hour after a full meal and died three hours later and was autopsied at once. We feel that this might be evidence of the fact that when an extensive lesion occurs in human eclampsia it may occur rather abruptly and not over a period of a long time such as is characteristic of so-called preeclampsia. The period of so-called preeclampsia may be regarded as a precursor in most cases and a sudden production of a marked liver lesion might precipitate the attack of eclampsia.

In concluding, although the lesions produced in this series are not entirely typical of hepatic lesions in eclampsia, we feel the mechanism of their production is similar to the lesion which occurs in the liver in human eclampsia and, therefore, we feel as we have stated in our first papers that we have further evidence that a hepatic lesion in eclampsia may result from a greater concentration of substances in the portal vein which can bring about thrombosis and which obviously must have their origin in great part from the intestinal tract. We also think this work further emphasizes the value of limiting the meat protein intake and the insistence on good intestinal hygiene in the patients in the last months of pregnancy, thereby averting at least the fulminating types of eclampsia.

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630 S. KINGSHIGHWAY.

(For discussion, see page 879.)

## FURTHER OBSERVATIONS UPON HYDATIDIFORM MOLE, WITH THE REPORT OF A CASE\*

BY EDWARD A. SCHUMANN, M.D., F.A.C.S., PHILADELPHIA, PA.

**I**N 1921 I proposed that certain hydatidiform moles be treated by abdominal hysterotomy, and if the findings warranted, by supravaginal hysterectomy. This procedure was not at all original, it having been advocated by Freund years ago and reiterated by Essen-Möller and Howard C. Taylor. Vineberg has suggested vaginal hysterotomy followed by manual removal of the growth and recently Turenne has reported a case in which abdominal hysterectomy was performed for this condition, the indication being great multiparity (ten pregnancies), evident mole, long and closed cervix, uncontrollable hemorrhage and intense acute anemia.

When presented to the profession, the above plan of treatment met with considerable disfavor, but as time goes on, there is more and more dissatisfaction noted in the literature with the conventional expectant plan of conducting these cases. Bland, for example, says "that expectancy is almost analogous to helplessness. Tardiness has not served to mitigate the primary mortality of the disease nor thwart the development of secondary chorioepithelioma with its widespread metastases. No disease of a potentially malignant nature, one of the chief characteristics of hydatid mole, is amenable to a process of watchful waiting."

It has been definitely established that the primary mortality of hydatid mole lies somewhere between 10 and 15 per cent (Gordon, 9 per cent in a small series, Findley, 10.5 per cent, Williams, 10 to 26 per cent, Hirst, 18 to 25 per cent). This primary mortality is due to hemorrhage, sepsis and toxemia, and does not take into account the secondary death rate from the possible development of chorioepithelioma, in which event the mortality rate rises to 50 or 75 per cent.

As to the frequency of this dread sequel, there is considerable difference of opinion, Findley finding 31.4 per cent, while Williams in a discussion of my paper in 1922, quotes Sunde in the *Acta Gynecologica Scandinavica* as concluding that while 50 per cent of chorioepitheliomas are preceded by moles, only 5 per cent of moles are followed by chorioepithelioma. In Lenarden's series of 49 cases of hydatidiform moles, 13 per cent developed this malignant change subsequently. On the other hand, there is evidence that this tumor is of uncommon occurrence, Symmers stating that not one case was discovered in 12,000 autopsies performed at Bellevue, while in Budapest where pathologists

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\*Read at a meeting of the Obstetrical Society of Philadelphia, Pa., March 7, 1929.

were searching for such cases for several years, none were found. Yet Lynch states that in eighteen months, seven cases were noted in 2,700 autopsies at the General Hospital of Vienna. At any rate one may estimate the general mortality from mole plus secondary chorioepithelioma as somewhere from 15 to 18 per cent. I submit that this represents one of the very high death rates from the complications of pregnancy and labor, and that if it be possible to do so, some plan of treatment should be devised which will materially decrease the gravity of the prognosis. Furthermore, the secondary morbidity in these cases is high, largely due to the common development of lutein cysts of the ovary in association with hydatidiform mole. In this connection Ewing quotes Patellani's statement that in 68 fully reported cases 62, or 91 per cent presented bilateral cystic changes. This proportion is probably too high, but, nevertheless pronounced cystic ovarian change is so common an accompaniment of hydatid moles as to constitute a definite pathologic feature of the cases.

The treatment of the condition may be divided into two general groups: Firstly, manual removal of the mole followed by curettage, the latter procedure being done even though the entire mass has been expelled spontaneously, the scrapings being examined by a competent pathologist to determine whether or not the tissues present positive or potential malignant change. Secondly, abdominal hysterotomy, preferably under local anesthesia at the time of the positive diagnosis of the presence of mole, the tumor to be completely removed under the eye at this time, and the necessity for hysterectomy determined by an inspection of the uterine musculature and the degree to which it has been invaded or injured by the mole. Immediate examination of frozen sections will materially aid in arriving at a decision. At this time lutein cysts of the ovaries, if present, may be appropriately dealt with.

To discuss these divergent methods in detail: The first has conservatism and simplicity to commend it, and in many instances, if coupled with careful observation of the patient for a year or more afterward and immediate recourse to radical surgery on the recurrence of bleeding, will undoubtedly serve to effect a cure in many cases, as it has in the past. However, it is precisely this plan of treatment which has been followed by the very high mortality as given above and therefore it would seem to be unsatisfactory.

As to the possibility of determining potential malignancy from curetting, pathologists are still divided, though there is a constantly increasing trend of opinion that this is impossible. Thus Hitschmann says positively that there are no morphologic criteria of value in establishing a prognosis. All moles must be regarded as rapidly growing tumors of embryonic origin and of potential malignancy. Caturani and others entirely corroborate this view, and it is a common experience of gynecologists to have a competent pathologist make a diagnosis of

early chorioepithelioma in a mole pregnancy, only to have the patient refuse the radical operation which such diagnosis entails and suffer no ill consequences.

During the manual or instrumental removal of mole via the cervical canal, furious hemorrhage may occur, not rarely to a fatal degree, perforation of the uterus is to be feared and a complete evacuation is problematical. These dangers are greatly enhanced, should the cervix be long and rigid as in a primipara and in those cases where the patient is a poor risk by reason of previous blood loss or infection.

The second plan of treatment, to which I am committed, may be outlined as follows: A preliminary blood transfusion is given in cases where there is marked anemia, the result of hemorrhage. Abdominal hysterotomy is performed, preferably under local anesthesia (morphine sulphate gr.  $\frac{1}{4}$ , scopolamine hydrobromide gr.  $\frac{1}{100}$ , hypodermically, one hour before operation, and then local infiltration with  $\frac{1}{2}$  per cent novocaine solution), or, if local anesthesia is not well borne, by a light inhalation anesthesia. The uterus may be opened on its anterior aspect with but little blood loss, the mole removed, and the uterine wall carefully inspected for areas of marked thinning, intramural hemorrhage, or widespread and deep invasion of the uterine muscle by the proliferative process. If the uterine muscle is in relatively good condition, the cavity may be swabbed with iodine, firmly packed with gauze, the end of the pack being thrust through the cervical opening, and the wound in the uterus carefully closed by layer suture, after which the abdominal incision is closed.

Where the uterus has undergone massive invasion with syncytial elements or where many hemorrhagic areas are present, supravaginal hysterectomy is the procedure of choice. At the same time the lutein ovarian cysts which so commonly accompany hydatidiform mole may be appropriately dealt with, by the removal or resection of one or both ovaries.

This method of treatment is especially indicated when the bleeding is profuse, the cervix rigid, and the patient near the climacteric. Abdominal hysterotomy has been criticized as a proper method of attack, by reason of the gravity of the operation and the probability that many uteri will be needlessly sacrificed as a result of such procedure. These criticisms are not well taken, because abdominal hysterotomy offers a far better opportunity to secure complete evacuation of the uterine contents under the eye than does mere manual exploration, and at the same time hemorrhage is under much better control. The dangers of perforation are eliminated, and the operator obtains an exact knowledge as to the condition of the uterus and the possible necessity for the performance of hysterectomy. The primary mortality of abdominal exploration is rather less than when the vaginal route is selected, and the morbidity is certainly no greater.

In those fortunate cases where the mole is loosely attached and is expelled spontaneously, en masse, without alarming hemorrhage, the uterine cavity may be explored with the finger and if its surface is found smooth, it may be hoped that no deep invasion has taken place and that no further treatment is necessary, save continued observation.

Radium therapy alone, or with deep x-ray is still sub judice, but inasmuch as both moles and chorioepitheliomas are made up largely of embryonal tissue, they should succumb readily to radiation and this adjuvant to more radical treatment should never be neglected.

The following case discovers many interesting points in the clinical manifestations and the problems involving these bizarre teratomas:

R. G., eighteen, married, was admitted to Chestnut Hill Hospital October 26, 1928, complaining of vaginal bleeding. The patient was a healthy young girl who was married at the age of sixteen and was delivered of a normal baby, by forceps, seven months before this admission.

Four months after her child was born she had a painless bleeding from the vagina which lasted a few days. About two weeks later she again had some vaginal bleeding unaccompanied by pain. There has been spotting and irregular bleeding until the day before admission when she had a profuse hemorrhage for which her physician advised hospitalization.

The family and past medical histories were irrelevant, the patient having always been healthy. Menses at fourteen years, twenty-eight-day type, flow lasting three to four days.

Physical examination: a thin Italian girl, nervous and apprehensive. The head, neck, heart and lungs presented no abnormalities. The abdomen showed the striae of a former pregnancy, and a smooth, rounded, fluctuating tumor extending from the symphysis to the umbilicus. This tumor strongly suggested a six months' pregnancy, although fetal parts could not be distinguished, nor were the fetal heart sounds audible. The patient insisted that she felt fetal life which in great measure influenced the diagnosis. X-ray examination of the abdomen was negative for a fetal skeleton.

On vaginal examination, the vagina was found cyanosed, the cervix soft, admitting one finger, with no effacement. A little blood escaped from the cervix after examination. The uterus was enlarged to the size of a six months' pregnancy, but no presenting part was palpated. The diagnosis lay between hydatidiform mole and placenta previa with hydramnion and, because of the insistence of the patient that she was aware of fetal movements, the latter condition was considered as the true one.

On the day after admission, the patient had a very free hemorrhage, which necessitated packing. On the following day there was more bleeding and the cervix being partially dilated, the examining finger detected an irregular mass in the lower uterine segment, which was recognized as a mole and under gas anesthesia, the entire mass was manually removed, the uterus firmly packed and 500 c.c. of blood administered by transfusion. All bleeding ceased and the patient made a good recovery, leaving the hospital in eight days. On examination for discharge, the uterus was in process of involution, both tubes were normal, the ovaries slightly increased in size.

On Oct. 21, 1928, less than one month after the expulsion of the mole, the patient was readmitted, complaining of nausea and severe pain in the right lower quadrant of the abdomen, with the presence of a distinct mass. The woman seemed in good general condition, no cardiac or pulmonary lesion being demonstrated.

There was slight rigidity over the right rectus and a large smooth mass, 8 to 12 cm. in diameter, was easily palpable in the right lower quadrant. The mass was tender to deep palpation and was quite freely movable. On vaginal examination, the cervix was found patulous, the uterus about twice normal size, and both ovaries had been converted into cystic masses easily 8 to 12 cm. in diameter. The cystic right ovary constituted the tumor felt on abdominal palpation.

The uterus was normal, the hemoglobin 65 per cent and the leucocytes 7500. A diagnosis of lutein cysts of the ovaries was made and laparotomy performed under nitrous oxide-oxygen anesthesia. The uterus was found to be of about twice the normal size, as one would expect after less than one month's involution. The tubes were normal, but both ovaries had been transformed into multilocular lutein cysts, the right 14 cm. in diameter and the left 12. Salpingo-oophorohysterectomy was performed, the convalescence was uneventful and the patient left the hospital on the fourteenth day after operation.

The pathologist reported bilateral lutein cysts of the ovary and an area of chorio-epithelioma, occupying the right side of the uterine fundus.

This case presents the following points of interest: A diagnosis of hydatidiform mole confused by the insistence of an intelligent multipara that she felt fetal movements. The very rapid development of large lutein cysts of both ovaries after expulsion of a mole. The presence of chorioepithelioma in the fundus uteri one month after the termination of a mole pregnancy.

1814 SPRUCE STREET.

*(For discussion, see page 885.)*

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**Beckers: Chronic Nephritis and Pregnancy.** Bruxelles-med. 7: 1237, 1926.

Pregnancy, undoubtedly, has a deleterious influence on chronic nephritis. This may be due to digestive troubles, in which an increased absorption of toxic products occurs in the intestines. They must be eliminated by the kidneys. In some cases the colon bacillus may pass by way of the blood stream to the kidneys thus causing a pyelitis or pyelonephritis. Again, during pregnancy, there is an increase of the nitrogenous products to be excreted, which is in direct opposition to the best treatment of chronic nephritis. Further, the uterine enlargement may cause circulatory disturbances. Finally, compression of one or both ureters will lead to retention of nitrogenous products.

Occasionally pregnancy may give rise to renal lesions called the nephritis of pregnancy. That fetal life is in some way bound up etiologically with these conditions is shown by the fact that the albuminuria often disappears upon intra-uterine death and before expulsion of the fetus.

Approaching trouble is manifested by retention of chlorides with edema. Here the treatment should be a salt-free diet. A straight milk diet is objectionable because of its high salt and fluid contents, also might cause a nitrogenous retention. In severe cases, only water should be allowed and free purgation instigated. In the milder cases the diet should be restricted to fruits and green vegetables. At times therapeutic abortion may become necessary. Where arterial hypertension is the outstanding feature, a strictly vegetable diet should be adhered to, combined at times with blood letting.

THEODORE W. ADAMS.

## ANALYSIS OF EIGHTY-FOUR CONSECUTIVE CESAREAN SECTIONS\*

BY JOHN COOKE HIRST, A.B., M.D., F.A.C.S., PHILADELPHIA, PA.

(From the Department of Obstetrics, Hospital of the University of Pennsylvania)

FROM January, 1926, to September, 1928, 1279 women were delivered in the maternity wards of the Hospital of the University of Pennsylvania, 84, or 6.5 per cent of whom were delivered by cesarean section. During this period of time 2700 women were delivered on the outside or South-Eastern Dispensary service of the Department of Obstetrics, of whom 89 were admitted to the maternity, and 14, or 0.51 per cent were sectioned. Eighty-four cesarean sections from a total of 3979 deliveries shows that 2.1 per cent of all cases under the care of this department required delivery by section, which represents a conservative attitude on this subject.

The sources and incidence of these deliveries and sections admitted to the hospital were as follows:

TABLE I

		TOTAL	CESAREAN SECTIONS	PER CENT
Prenatal Clinic	(55%)	704	33	4.7
Staff	(25%)	320	25	7.8
Outside Physicians	(10%)	128	12	9.3
South-Eastern Dispensary	( 7%)	89	14	15.8
Receiving Ward	( 3%)	38	0	0
		1279	84	

This table shows that we considered it necessary to operate upon one out of every 21 women who came to us for careful prenatal observation.

The reasons for performing the cesarean section are shown in Table II.

These operations were done by the regular staff of the University Maternity comprising 6 individuals, 3 of whom accounted for the large majority of the sections. There is therefore listed a number of procedures which are briefly explained under Table III.

At this point, certain items of procedure must be mentioned in order to qualify the accompanying records. The following methods have been fairly uniformly employed by our clinic:

1. Preoperative preparation does not include morphine.
2. Anesthesia in most instances is gas-oxygen, with a minimum of ether. Only two cases were performed under local anesthesia.

\*Read at a meeting of the Obstetrical Society of Philadelphia, Pa., March 7, 1929.



TABLE II. INDICATIONS FOR CESAREAN SECTION

1. Contracted Pelvis	45
a. Elective sections:	
1. Deformed pelvis	6
2. Deformed pelvis with previous section	19
b. Emergency sections:	
1. Dystocia in deformed pelvis	17
2. Dystocia in deformed pelvis with previous section	2
3. Deformed pelvis with placenta previa	1
2. Indications Other Than Contracted Pelvis	39
a. Elective sections:	
1. Previous section with disproportion	5
2. Previous dystocia with fetal mortality	3
3. Disproportion	1
4. Obstructing pelvic tumor	3
Ovarian cyst, 1; Myoma Uteri, 2.	
5. Habitual death of fetus	1
6. Sacculation of uterus from fixation by previous operation	2
7. Cardiac disease	1
8. Pulmonary tuberculosis	1
b. Emergency sections:	
1. Dystocia	16
Disproportion	6
Disproportion and previous section	1
Sacculation of uterus from fixation by previous operation	4
Cervical dystocia in elderly primiparae	3
Placenta previa complicating labor	1
Inertia uteri due to pulmonary tuberculosis	1
2. Placenta previa	2
3. Abruptio placentae	1
4. Eclampsia	1
5. Intestinal obstruction	1

TABLE III. TYPES OF CESAREAN OPERATIONS PERFORMED

	ELECTIVE	EMERGENCY	TOTAL
High classical	17	17	34
Low classical	12	8	20
Kerr cervical	8	6	14
Beek cervical	3	9	12
Marsupialization	0	2	2
Porro	2	0	2
Total	42	42	84

3. No preliminary cervical dilatation in the elective operations.

4. No intrauterine packing in any case.

5. Preliminary mercurochrome gauze vaginal packing introduced while the patient is on the table and removed as soon as operation is ended, is used in neglected or examined cases.

6. All fundal uterine incisions are sutured by Piper's (or modified) special subserous water-tight gut suture, giving freedom from distension and adhesions somewhat similar to the cervical operation.

7. Abdominal wound suturing comprises the usual procedure, using derma skin and 3 or 4 silkworm-gut tension sutures.

8. Aseptic ergot and pituitrin are administered as the operation is well begun.

“High Classical Cesarean Section” refers to the usual operation, with an abdominal incision  $\frac{1}{3}$  above and  $\frac{2}{3}$  below the umbilicus, and the common miduterine incision; sutured in a special manner described later.

“Low Classical Cesarean Section” means a low “gynecologic” abdominal incision, with a vertical uterine incision as low as possible (to the bladder), closed by special suture.

“Kerr Cervical Cesarean Section” is the now well-known procedure illustrated in this article. (See Figs. 1, 2, 3, 4, 5, 6.)

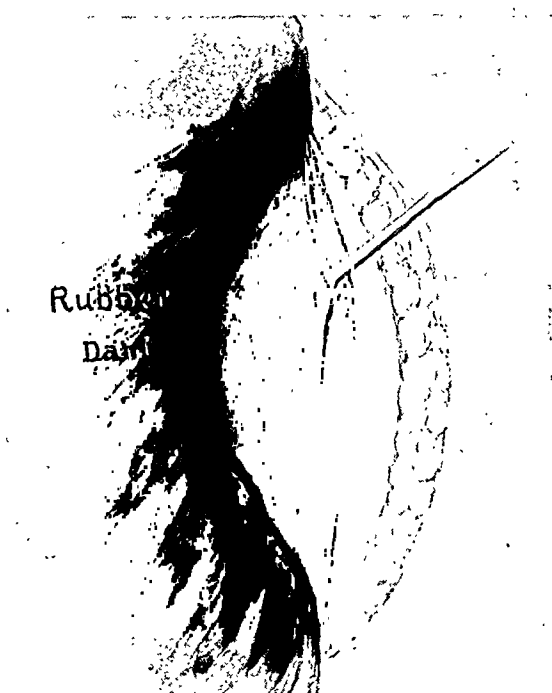


Fig. 1.—This and the following figures show the author's modifications in the preliminary and final stages of the Kerr operation. Wound protection

“Beck Cervical Cesarean Section” is the original Beck technic, with one transverse serous uterine incision and one longitudinal muscular incision.

“Marsupialization Cesarean Section” refers to the extraperitoneal technic of B. C. Hirst, whereby uterine peritoneal flaps mobilized by low vertical incision are attached to the corresponding cut parietal peritoneal edges before the uterine musculature is incised.

TABLE IV. NUMBER OF PRIOR CESAREAN SECTIONS

1. Total number of sections		84
2. Total in which previous sections were performed		29
One previous section	20	
Two previous sections	7	
Three previous sections	2	

Our results are given exactly as noted, without any exclusions. All cases admitted with temperature are included under operative morbidity. The chief disappointment that we experienced was in three cases of peritonitis, unfortunately twice in elective cases, one of whom was a most difficult repeat operation and bad surgical risk.

We feel justified in explaining some of the mortality under the dys-

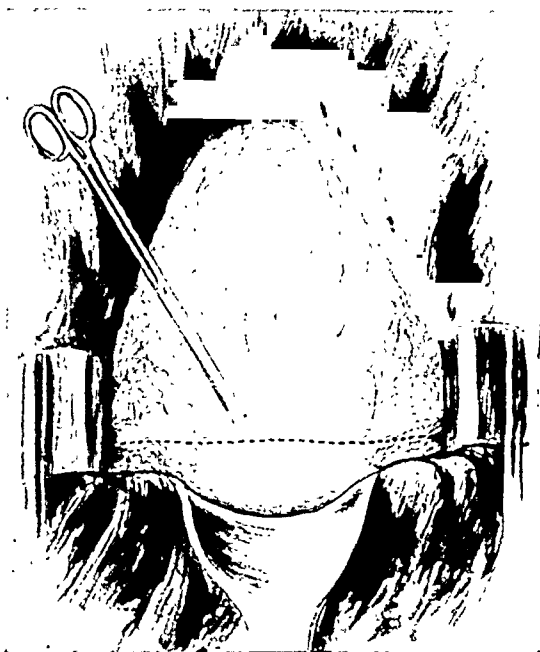


Fig. 2.—Incision in peritoneal fold over head and above bladder.

TABLE V. MATERNAL AND FETAL MORTALITY

1. Total number	84
2. Maternal mortality (all cases)	7 (8.33 per cent)
Hemorrhage (ablatio)	1
Peritonitis	3
Shock	1
Eclampsia	2
3. Mortality in elective group:	
Total elective operations	42
Total mortality	2 (4.76 per cent)
Peritonitis	2 (1 Kerr Section with fixation and sacculation of the uterus with diabetes.)
4. Mortality in emergency group:	
Total emergency operations	42
Total mortality	5 (11.9 per cent)
5. Fetal mortality (total)	17 (20 per cent)
Prematurity	3
Intracranial hemorrhage	7 (long labors)
Maceration (abruptio, eclampsia)	2
Placenta previa	3
Adenoma, thyroid	1
Narcosis	1 (morphine)

tocia group by noting a large percentage of dry and prolonged labors occurring before hospital admission, shown in Table VI.

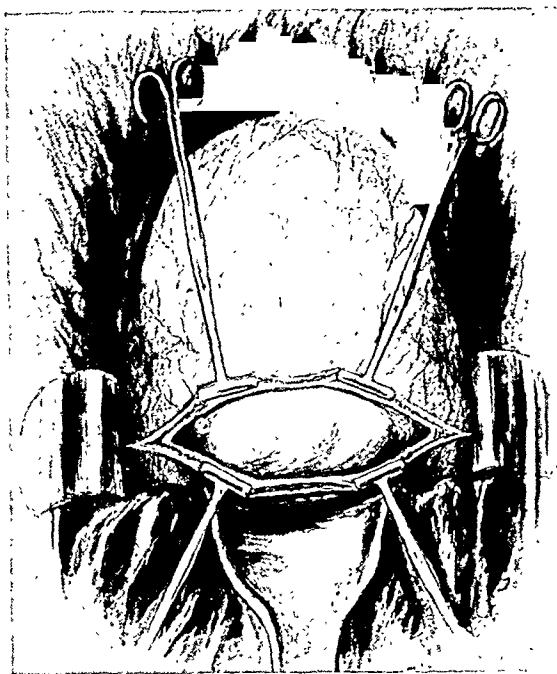


Fig. 3.—“T” clamps on thin uterine muscle to control hemorrhage if present. Shows membranes herniated.

TABLE VI. CESAREAN SECTION IN DYSTOCIA GROUP

1. Total number			35
Contracted pelvis	19	Inertia uteri	1
Disproportion	7	Sacculation	4
Cervical dystocia	3	Placenta previa	1
2. Average number of hours of labor before section			29.1 hours
3. Average number of hours membranes ruptured (15 cases)			25.2 hours
4. Average number of vaginal examinations (29 cases)			2.2
5. Number of patients febrile preoperative			16
Classical	8		
Cervical	8		
Extraperitoneal	0		
6. Types of Cesarean Section Employed:			
Low classical	6		
High classical	12		
Kerr cervical	6	Fundal = 18	
Beck cervical	9	Cervical = 15	
Marsupialization	2		
	35		
7. Maternal mortality (dystocia group)			2
Shock	1 (Beck operation)		
Peritonitis	1 (High classical operation)		
8. Febrile morbidity (eliminating 3 day postoperative fever)			25 (71 per cent)
(See explanation, Table VII, item 2.)			
Eliminating causes other than puerperal fever, as			
pyelitis, mastitis, pneumonia, tuberculosis, (12)			13 (37 per cent)
Fundal operation morbidity, out of 15 = 40 per cent			6
Cervical operation morbidity, out of 18 = 39 per cent			7



FIG. 4.—Uterine muscle closure, with 3 or 4 stay sutures and tier continuous suture.

TABLE VII. TOTAL FEBRILE POSTOPERATIVE MORBIDITY

1. Total number	85
2. Total febrile morbidity postoperative (Excluding postoperative reaction)	48 (57 per cent)
a. Excluding causes other than puerperal fever:	
Pyelitis	9
Pneumonia	3
Pulmonary tuberculosis	1
Mastitis	4
Hypodermic abscess	1
Pleurisy	1
Eclampsia	1
	(20) 28 (33 per cent)
b. Causes of puerperal fever (Febrile postoperative morbidity)	
Endometritis	19
Lochial block	6
Peritonitis	3
3. Puerperal fever analysis:	
a. Dystocia group, of 35 there were febrile	15 (43 per cent)
Fundal operation (of 18)	7 ( 39 per cent)
Cervical operation (of 15)	6 ( 40 per cent)
Extraperitoneal operation (of 2)	2 (100 per cent)
(Marsupialization)	
b. Elective group of 42 there were febrile	11 (26.2 per cent)
Fundal operation (of 29)	6 ( 20 per cent)
Cervical operation (of 11)	5 ( 45 per cent)
Porro operation (of 2)	0 ( 0 per cent)
c. Emergency group, of 42 there were febrile	17 (40 per cent)
Fundal operation (of 25)	9 ( 36 per cent)
Cervical operation (of 15)	6 ( 40 per cent)
Extraperitoneal operation (of 2)	2 (100 per cent)

It should be borne in mind that the University Maternity morbidity standard is much more strict than most, because any woman showing

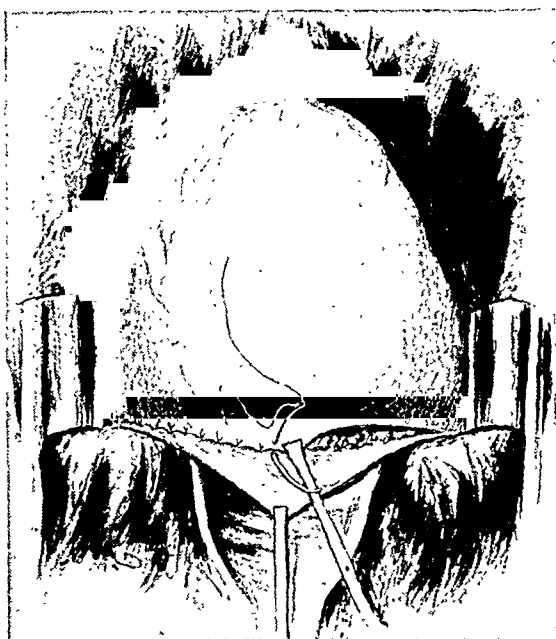


Fig. 5.—Tacking down upper serous flaps.

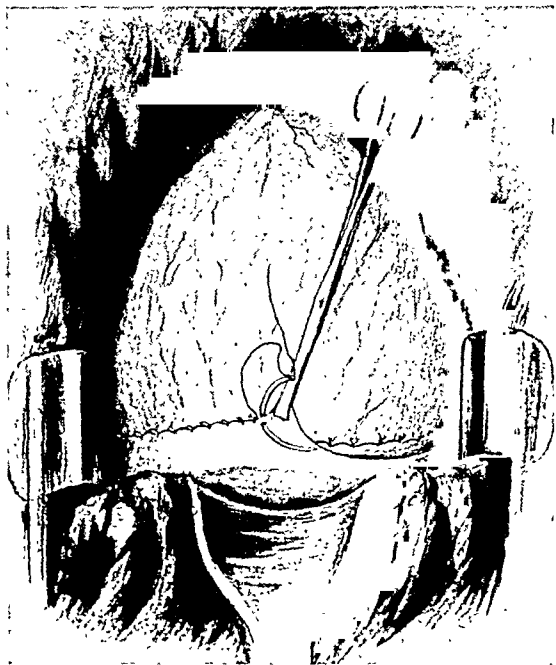


Fig. 6.—Continuous overlapping of lower serous flap with the fine inverting suture.

a temperature of  $100^{\circ}$  F. twice in any twenty-four-hour period, taken every four hours, *no causes excluded*, is considered morbid from child-birth.

Wound complications are determined by the American College of Surgeons Classification, briefly as follows: Types "A" and "B" may not be true infections, and are mainly serum collections, superficial pus pockets, hematomas and the like. Type "C" signifies any wound discharge giving a positive culture; any fascia defect; or any wound condition causing overtime hospitalization. Such complications were:

TABLE VIII. WOUND COMPLICATIONS

1. Total number of sections, elective—42, emergency—42	84
2. Total wound complications	9 (10.7 per cent)
a. Elective group	3 A—2 B—0 C—1
Emergency group	6 A—1 B—4 C—1
b. No labor prior to operation	3 A—2 B—0 C—1
Section during labor	6 A—1 B—4 C—1
c. Fundal operations	5 A—3 B—1 C—1
Cervical operations	4 A—0 B—3 C—1

We should like to supplement the foregoing records with a brief statement of a personal series of 85 additional consecutive cesarean sections from 1920 to 1928, with two deaths, one from peritonitis, and the second at two weeks from metritis after myomectomy. In this series were:

One ruptured uterus, 18 hours duration (recovered).

Three cases operated on after induction of labor by bougies and bag (recovered).

Other complications such as ovarian cyst, chronic appendicitis, tuberculosis, cardiac disease, etc.

Two cases of macerated fetus, wherein the cervix did not permit vaginal section (recovered).

## COMMENT

In choosing between the low classical cesarean with overlapping (Piper) serous suture, the Beck cervical, and the Kerr cervical, arguments appear to favor the Kerr operation in many types of cases, for the following reasons:

1. There is usually little hemorrhage.
2. It is easy and rapid.
3. Immediate and remote recovery is quite as satisfactory as in the Beck cervical technic.
4. Uterine suturing is very simple.

The illustrations of the Kerr cesarean section show the technic that has given us the best results. The only question that may be raised at the present time in regard to this operation is whether the scar will withstand subsequent pregnancy and possibly labor as well as that of other types of procedure. This question cannot be answered until sufficient time has elapsed for three or more operations of the Kerr type to be performed on the same individual, although it is reasonable to assume that ultimate results will also be satisfactory.

## REPORT OF A CASE OF OVARIAN PREGNANCY

BY ABRAHAM STRAUSS, M.D., CLEVELAND, OHIO

*(From the Surgical Service of Mt. Sinai Hospital)*

I BELIEVE that this case fulfills the criteria on which to base a diagnosis of ovarian pregnancy as laid down by Spiegelberg in 1887 and also has the embryo in the sac.

Patient, A. R., white, aged thirty-three, married six years, admitted to Mt. Sinai Hospital, August 10, 1928, complaining of vaginal bleeding and abdominal pain of two weeks duration. She always had had good health. Has two children living and well. Both labors were normal. She had no miscarriages. Menses were always regular, every twenty-eight days, flow five days, moderate in amount, not painful. Last menstrual period May 17, 1928. Previous menstruation April 18. No period in June or July until present illness.



Fig. 1.—Ovary bisected. Gestation sac containing blood clot and embryo attached to placenta by umbilical cord.

On July 24, 1928, the patient had severe, sharp, needlelike pains throughout her entire abdomen, radiating to the back. She fainted at the onset of these pains. At the same time she noticed vaginal bleeding. It was profuse at first but gradually subsided and the next week she only spotted. On one occasion she passed a large clot. Two days before admission the abdominal pains were again severe, radiating to her shoulders. Morphine was given to control the pain. Vaginal bleeding increased in amount in the few days before admission. At the same time she experienced severe burning pain with micturition.

Abdominal and vaginal examinations on admission yielded the only positive findings. A definite prominence was noted in the hypogastrium. The whole lower abdomen was tender and slightly spastic. The cervix was soft, admitted one finger. The uterus was enlarged and tender. Over the top of the fundus and extending into the left fornix and indefinitely into the culdesac there was a tender mass about three inches in diameter. It was difficult to make out this mass separate from the uterus. There was a bloody discharge from the uterus. Blood count: R.B.C. 4,900,000; Hgb. 70 per cent; W.B.C. 5,600.



Blood pressure 120/70. Pulse 90. Temperature 98.6. Wassermann and Kline precipitation tests negative. Diagnosis of ectopic pregnancy was made.

*Operation.*—Nitrous oxide and ether anesthesia. Midline hypogastric incision. Uterus was the size of a two months' pregnancy but quite firm. No nodular growths present. Right tube and ovary were normal. The left ovary was replaced by a large purplish, red tumor mass about three inches in diameter which was quite firmly bound down on the posterior surface of the broad ligament and the sigmoid by numerous adhesions. Left fallopian tube was apparently normal except it had become more or less flattened out due to the pressure from the ovarian tumor. The ovarian tumor was freed by finger dissection. The ovarian pedicle was clamped, severed, and the left ovarian tumor removed with the tube. Section of this tumor mass showed the presence of a primary ovarian pregnancy. The ovarian pedicle was ligated with No. 2 chromic catgut. The cecum was delivered and a long appendix, about four inches in length, was severed from its mesentery and removed by cautery, purse string method. Vessels of mesentery ligated.

*Examination of specimen.*—Ovary measured approximately 9 by 6.5 by 7 cm. The external surface bluish red, covered here and there by tags of fibrous tissue. Section shows a gestation sac, approximately 4 cm. in diameter, in which there is an



Fig. 2.—Ovary. A. Corpus fibrosum. B. Chorionic villi ovary.

embryo measuring 11 mm. crown-rump length (approximately forty-two days pregnancy). There is an umbilical cord attaching the embryo to the placenta. The placental tissue has almost entirely replaced the normal ovarian tissue and measures approximately 18 to 25 mm. in thickness. There is fluid and blood clot in the gestation sac.

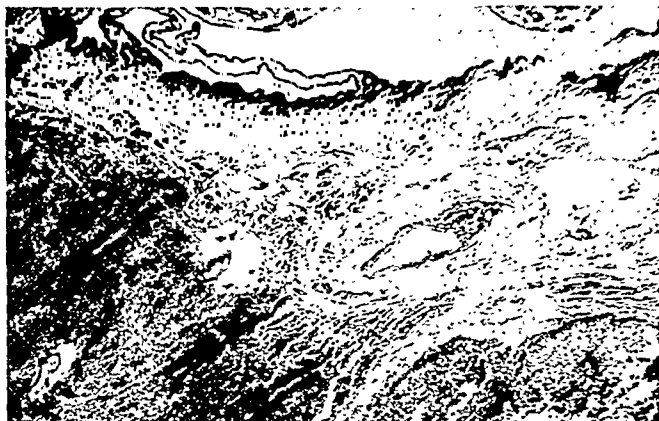
*Appendix:* Distal 8.5 cm. diameter approximately 7 mm. Serosa is covered in distal half by reddish-brown, friable material, apparently blood clot. There is considerable injection of distal half of appendix. On repeated section lumen continues to within a few mm. of tip, moderately dilated, contains brown fecal material. There is slight edema of all coats.

Section of the appendix shows a diameter approximately 8 mm. Lumen moderately dilated, contains fecal material. There is some increase in eosinophiles, otherwise inner coats not appreciably altered. Serosa is edematous, covered by a layer of fibrin in which there is a moderate number of wandering cells. There are also a number of islands of typical decidual cells attached to serosa. Nuclei of decidual cells well stained, cell outlines well defined.

Two additional sections show a similar picture except that there is no decidual reaction in serosa.

One section of ovary shows no recognizable ovarian tissue. There are a number of chorionic villi widely separated by red blood cells. Villi show early degenerative

changes, a number blue stained. Syncytium two layers in thickness. There are scattered decidual cells present, nuclei of which are well stained. Cell boundaries poorly defined. Another section shows in addition typical ovarian tissue surrounding chorionic villi. All of the villi in the section show degenerative changes of moderate to considerable degree. A number are present in and about dilated thin-walled blood vessels, in the walls of which there are large spindle cells apparently involuting decidual cells. Some of the vessels appear ruptured and there is blood clot in the neighborhood.



X.

Fig. 3.—Fallopian tube with chorionic villi outside at X. No reaction within the tube.

Fallopian tube: Two sections. Distal portion shows moderate scarring and leucocytic infiltration of all coats, the lumen, somewhat dilated, contains blood clot. In the outer coats, in places, there are groups of chorionic villi, majority showing considerable degeneration. In places, there is regional hemorrhage. In places, there are large spindle cells, apparently involuting decidual cells. In places, chorionic villi are present within dilated thin-walled blood vessels.

*Final Diagnosis.*—Ovarian pregnancy of approximately forty-two days' duration with small amount placental tissue.

The patient made an uneventful recovery and was discharged from the hospital on the fourteenth day after operation.

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## THE CARE OF THE LACTATING BREAST

BY FRED B. SMITH, B.S., M.D., HOUSTON, TEXAS

THE subject considered in this paper is the most generally neglected phase of the obstetrician's obligation to the parturient patient. After having guided her safely through the dangers of her antepartum period, exercised his skill and judgment at the time of delivery, and given a few words of advice in regard to her postpartum activities, he usually considers his responsibility ended. Yet, at this time the mother's breasts are undergoing changes which may result in more physical pain, a greater constitutional reaction, and a longer convalescent period than is caused by parturition itself. Often the infant is deprived of his most favorable food supply. The physician is embarrassed by being forced to treat a condition which is due to his, or his agent's, negligence; therefore, he must maintain a policy of watchful expectancy until the mother is safely past the danger of breast complications.

The care of the breast during pregnancy needs very little consideration, for we may say that a normal breast needs no treatment. Nature herself is preparing the gland for its future task; and, unless some definite indication for interference arises, the process should be left strictly alone. Proprietary lotions and oils sold to the mother are worse than useless. No beneficial results come from wearing tight brassieres or from massaging. Indeed, the latter is often harmful, as it results in a hyperplasia of the fibrous supporting structures of the breast at the expense of the secreting portions. Nipples, which early in pregnancy seem depressed, usually become protuberant during the later months. The nipple which is frankly inverted yields to manipulation so rarely, and the manipulation is accompanied by such danger of injury and infection that the attempt is not justifiable. The mother with such nipples should be advised to forego placing her baby to the breast from birth, as it is seldom that an infant can obtain the milk satisfactorily from an inverted nipple, and practically an impossibility to prevent breast complications if it persists in the effort. Fissures and abrasions of the nipple occurring during pregnancy require the same treatment as those occurring postpartum.

Ordinarily the passive breast of pregnancy remains in its state of simple generalized hyperplasia for several days following parturition. Then, in a few hours, it becomes one of the most active organs of the body. Its venous and lymphatic stasis, its tumefaction and hyperemia, the acute dilatation of its tubules and acini, and the hypertrophy of its lobules, all invite bacterial invasion. It is at this time that the obstetrician must be most observant and prophylaxis most scrupulously practiced.

Prophylaxis against bacterial invasion begins with the first attempt of the infant to nurse. This occurs, usually, from six to twelve hours after birth. As we cannot free the infant's mouth of bacteria, we direct our efforts toward the mother's nipple, seeking to prevent the entrance of bacteria into the breast. Numerous agents have been suggested for this purpose. Of these, a saturated solution of boric acid is the most universally accepted, being applied to the nipple before nursing, or both before and after. Yet, such a solution has no advantage over plain water, as Van Dolsen, of Philadelphia, has shown that the various strains of staphylococcus, the most frequent invader of the breast, grow readily on cultures of boric acid solution. As it gives rise to a false sense of security, boric solution should be abandoned. In 1926, Van Dolsen advanced the idea of using a modified Dakin's solution; that is, a one-tenth of 1 per cent solution of sodium hypochlorite in sterile water. I have observed the use of this for over a year and regard it with great favor. In 250 patients on whom it was used, there developed one case of breast abscess (0.4 per cent). The same obstetricians delivered 850 patients on whom boric solution was used, and breast abscess developed nine times (1.06 per cent). The modified Dakin's solution is easy to apply. The solution, on a small sponge or pledget of cotton, is placed in contact with the nipple for one minute immediately preceding the act of nursing. After taking the infant away, the nipple is sponged with sterile water to remove the film of milk left by the infant's lips. When this technic was begun, the principal objection offered was that the chlorine content of the solution would cause an acute dermatitis of the nipple and areola. So far, this complication has never been encountered, nor has there been noted any injurious effect on the baby. The solution should be freshly prepared, tightly corked, and kept in a dark place to prevent its becoming inert.

During the time that lactation is being established, the most frequent complications arising are nipple fissures, excessive sagging of the breast, engorgement, and "caking," the latter being only a pronounced degree of engorgement. Of these, fissured nipples demand the greatest consideration, for they are the portals through which bacteria enter the lymph channels and gain access to the deeper structures of the breast. They are minute breaks in the epithelial covering of the nipple, which may or may not bleed, and which are practically always the result of unavoidable trauma to the nipple by the lips and gums of the infant. Their detection is the signal for vigorous treatment. First, we strive to keep them aseptic by allowing the baby to nurse through a sterile glass nipple shield, or by emptying the breast with a pump. Tincture of benzoin compound is applied to the nipple and areola after each nursing. The fissures may be touched with 10 per cent silver nitrate solution but care must be taken that the solution is applied only to the fissures, and this is easily done by using a toothpick as an

applicator, moistened with the silver nitrate. Exposure of the nipple to ultraviolet light, or sunlight, hastens the healing process. Usually the fissures yield to this plan of treatment within thirty-six to forty-eight hours. If they do not, it becomes necessary to place the nipple in a state of absolute rest. This is secured by applying a snugly fitting breast binder, stopping the nursing or pumping, and avoiding all manipulation of the breast. Pain and engorgement may be controlled by codein and the intermittent application of ice bags. Meanwhile, the baby may be given one of the artificial foods. This treatment may be safely kept up for forty-eight to sixty hours. If the fissures are still present at the end of that time, the baby must be permanently placed on a formula, as it would be folly to permit nursing while they are still present, and further treatment results in a drying up of the breast. However, it is rarely necessary that nursing be abandoned.

Excessive sagging, engorgement, and "caking" may be considered together, as they are all interrelated. Stasis of the venous and lymphatic flow, following the bending of the lactiferous tubules, is their common etiologic factor. These conditions are extremely painful, but of more importance is the fact that a breast in the state of engorgement is also in the state of least resistance to bacterial invasion. It is during this period that bacteria most frequently pass through the nipple and begin their journey inward. The treatment of these conditions begins, and is usually successfully ended, by securing mechanically corrected posture. When the gland is restored to its normal anatomic position, the engorgement rapidly subsides. The breasts are lifted upward and inward and pushed closely together in the midline. This should be done without compression of the breasts, using a binder twelve inches wide. The binder's tendency to wrinkle is lessened by making it of six to eight thicknesses. It should fit snugly, but not tightly, and the upper one-third need not be pinned. The entire surface to be covered should be powdered, and soft lint or cotton should be placed at the sides and between the breasts to prevent chafing. A saline cathartic is given; the baby is temporarily removed from the breast, and morphine may be given. If the engorgement is not relieved, ice bags may be applied. They are applied for two hours, then taken off for two hours; and this schedule is maintained for twelve hours after the temperature has dropped to normal. In the absence of infection, or if the infection is going to respond to this treatment, the breasts will become softer and free from pain in a few hours.

A word of caution should be given here against manipulating an engorged breast. There is a widespread belief, especially among the laity and practical nurses, that the condition is caused by an accumulation of milk, and that relief follows removal of that milk. The milk is sometimes removed by pumping, oftener by massage. In skilled hands and under the best conditions this affords only temporary relief, for

the underlying cause is not corrected. And to subject a breast that is already in a pathologic condition to the assault of a determined woman, intent on expressing milk, assures the patient of further complications. Tissues already taxed to the point of lowered vitality are traumatized, bacteria are drawn deeper into the gland, and trouble ensues—usually abscess. Except for the treatment mentioned above, an engorged breast should be undisturbed.

In the presence of infection the traumatized, engorged breast develops one of the four types of acute mastitis: namely, subareolar, parenchymatous, interstitial, or submammary. Of these, the parenchymatous type is by far the most common. Since the treatment of all four is essentially the same, the differential diagnosis may be passed over. The breast has been properly supported, ice has been applied, the saline purge administered, and the breast has not received insult by massage or pumping or nursing. Yet, after forty-eight hours, there is no improvement in the patient's condition, or her symptoms are aggravated. The fever becomes alarming. Chills appear. All the cardinal symptoms of suppuration are noted. Then we know that somewhere in the gland an abscess is forming. As soon as this is evident, the ice bags are removed and hot, wet applications are substituted, care being taken not to burn the skin. These applications are continued for twenty-four hours. At the end of that time the abscess is usually palpable, and drainage should be established. If the incision is delayed, the patient's toxemia becomes alarming, and the pus burrows into other lobes or even to the areolar tissue beneath the breast. The site chosen for the incision should be directly over the abscess, and extend radially from the nipple to avoid severing the lactiferous tubule. The incision should extend at least a half-inch on either side of the abscess, as it is inclined to early closure. The finger which is introduced into the cavity explores and breaks down any septa found walling off other pockets of pus. In this way, separate incisions for adjacent abscesses are avoided. Gentle pressure may be applied to the breast to aid in evacuating the pus. Forcible evacuation, however, is followed by a severe chill and a sharp rise in temperature, and should be avoided. After all the septa have been destroyed, one or more rubber tissue drains, of liberal size, are placed in the abscess. They are left undisturbed for forty-eight hours, and are then gradually withdrawn a little each day. Hot, wet, antiseptic dressings are applied to the breast, and the damage heals with surprising rapidity. This operation is an extensive and exceedingly painful procedure and, for the sake of the patient's comfort and the thoroughness of operation, should never be attempted with local anesthesia alone. Ethylene gas is the anesthetic of choice for this operation.

There remain to be considered a few other problems, such as inverted nipples, the occasionally encountered necessity for drying up the milk,

and the very frequent problem of deficient secretion. Concerning inverted nipples there are two conflicting interests: that of the mother and that of the child, and both are of major importance. Pediatricians are unanimous in the opinion that the results of no other food equal or approach in freedom from nutritional disturbances, those given by milk from the mother's breast. The infant deprived of this food falls victim to a rapidly progressing acidosis. Pediatricians also tell us, and vital statistics support them, that the first ten days of the infant's life comprise its most hazardous period; that after having passed the dangers of this time, it has more or less mastered its completely changed environment and more readily responds to therapeutic and dietary measures. On the other hand, we must consider the mother with inverted nipples. Allowing her baby to nurse most probably will initiate mastitis and breast abscess. To meet this extraordinary situation, I favor a plan of compromise. The milk is taken from the breast by means of a sterilized hand pump, or if the patient is in a well-equipped maternity hospital, by the electric pump, and given to the baby by bottle. This is continued for twelve days. Meanwhile, one of the artificial foods is being gradually substituted for mother's milk. At the end of this time the infant is given artificial food only, and the breasts are dried up as a prophylactic measure to forestall the inevitable abscess. This plan gives the infant his most favorable food during his critical period. But it is not without danger to the mother, for with the slightest break in aseptic technic, mastitis may develop and end the entire procedure. However, it is always worthy of trial; and with the aid of intelligent nurses, will give excellent results.

Other than as a prophylactic measure in the case of inverted nipples, there are several indications for drying up the breast. It may be occasioned by disease of the mother, as a severe anemia or pulmonary tuberculosis. It becomes necessary following death of the infant or stillbirth. The means of accomplishing this have changed considerably in the past few years. Formerly, it was a tedious and painful process, characterized by alternate periods of engorgement and of the emptiness following massage or pumping. Mastitis was a frequent complication. With our present plan of treatment the worst part is over within twenty-four hours. A wide tight binder, which both supports and compresses the breasts, is applied. Over this, ice bags are applied and allowed to remain in place without intermission. The patient's liquid intake is restricted, and a saline purge is given. In six or eight hours the breasts become painful, and this symptom may be relieved by one-half grain of codeine. A second dose is seldom necessary, for within a few hours the breasts become softer and the pain disappears. Massage and pump are not permitted. The ice bags are removed after twenty-four hours, but the binder is left in place for several days. This plan of treatment has the advantages of being quick, efficient, and in this series, has not been followed by abscess or mastitis.

A deficient secretion of milk is a complaint by no means uncommon. It may be a temporary or a permanent phenomenon. Very often following a strong emotional upset in the mother, it is noted for two or three days. The permanently deficient type is usually noted in successive generations of mothers. Concerning the relief of this condition we know very little. Drugs and glandular extracts have been of no value. Dietary measures, while helpful, give only uncertain results. Overfeeding causes a gain in weight of the patient, and an actual decrease in quantity of milk. Hence, the daily caloric intake should be that normally required for the woman, plus not more than six or seven hundred calories for milk. The fluid intake should be generous. Stimulation of the breast by massage is no longer recommended by Dr. J. B. DeLée,\* who has found stimulation by the electric pump more satisfactory and less dangerous. The obstetrician cannot give up the time required for massage and, if administered by a nurse or neighbor, it usually results in a severe mastitis. The dairyman knew long before the physician that repeated incomplete emptying of the gland caused a progressive decrease in the quantity of milk secreted. It is logical, then, to empty the breast further by means of the pump after the infant has ceased his nursing efforts. This measure sometimes gives surprisingly good results. However, with the diet properly regulated, there is probably no stimulant as good as the vigorous nursing of a hungry infant.

In conclusion, I wish to say that the principles expressed in this paper are based on observation of eleven hundred consecutive cases delivered by Drs. H. W. Johnson and R. A. Johnston and myself. That they are of value is evidenced by the fact that in the eleven hundred mothers, abscess of the breast developed only nine times—an incidence far below the average. Even this ratio will be improved, most likely, with the continued use of sodium hypochlorite solution as a breast antiseptic. The salient features which have been expressed are cleanliness, support, alertness on the part of the physician, and the avoidance of trauma. At no time is massage of the breast justifiable. Closer observance of these widely neglected principles will give results not generally attained in the care of the lactating breast.

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\*Personal communication from Dr. J. P. Greenhill.



## SECONDARY ADENOCARCINOMA OF THE OVARIES FROM THE JEJUNUM

BY MELVIN A. ROBLEE, B.S., M.D., ST. LOUIS, MO.

*(From the Department of Obstetrics and Gynecology, Washington University  
Medical School)*

MUCH has been written on the subject of scirrhus carcinoma of the ovaries secondary to some gastrointestinal carcinoma. The Krukenberg's tumor of the ovary, with its special pathology, has long been recognized as secondary to gastrointestinal cancer. Major has made quite an exhaustive study of this type of tumor and concludes that whenever reference to it in the literature as a primary carcinoma has been made, the observer has failed to definitely exclude a gastrointestinal primary site.

Taylor has reviewed the literature of malignant and semimalignant tumors of the ovary. He reports scirrhus carcinomas of the ovaries secondary to some gastrointestinal carcinoma that either show or do not show a resemblance to the peculiar signet ring scirrhus type called Krukenberg. Several cases of secondary carcinoma have occurred in cystic or papillary ovarian structure, and he feels that the presence or absence of "signet ring" pathology has little to do with the subject of metastatic gastrointestinal ovarian malignancy.

Stone, in discussing metastatic carcinomas in the ovary, states the route of metastasis is most often by direct extension through the retroperitoneal lymph nodes by permeation, or by retrograde transportation, or by peritoneal implantation. The latter is quite common during the period of active functioning of the ovaries because of circulatory changes and trauma to the surface from ovulation. This is most often seen when there is peritoneal metastasis particularly in the culdesac. Experimentally it has been shown that carbon particles introduced into the upper peritoneum will gravitate to the culdesac, and collect on the surface of the ovaries.

Stone also points out that many observers state that there is a continuous course of lymphatic invasion through the lymph vessels and nodes behind the structures of the upper peritoneal cavity into the retroperitoneal lymphatics on both sides of the aorta to the enlarged lumbar nodes and then, by a reverse current in the spermatic lymph vessels, the cancer cells are carried through the hilum into the ovaries. By this route there might be no peritoneal metastasis.

Schaeffer thinks metastasis may occur along the reverse route and cites a case to substantiate his view.

Soper in 1909 reviewed the work of Schlieps and added two cases of primary carcinoma of the jejunum and ileum. Schlieps collected 38 cases from 1867 to 1908 and to this number added 5 cases from the Breslauer Surgical Clinic, totaling 43 cases. Nineteen of these were carcinoma of the jejunum. Soper found 12 cases of carcinoma of the small bowel not mentioned by Schlieps. Several of these were in women but there is no report of metastasis. Soper again in the *Journal of the A. M. A.* (92: 286, 1929) reports a case of an annular carcinoma about ten inches below the duodenojejunal junction. The patient died of metastasis six months after operation for resection.

In view of what has already been written on secondary carcinoma of the ovaries, I believe that a report of a case of true adenocarcinoma of the ovaries that was secondary to an adenocarcinoma of the jejunum would be of interest, especially since there was no other metastatic cancer. Carcinoma of the jejunum is a very rare malignancy. That this rare type of gastrointestinal carcinoma should metastasize in its true form to the ovaries in which there was neither cystic nor papillary changes present is of special teaching significance, particularly as the endometrium, tubes, and cervix showed no cancer.

A white woman thirty years of age presented herself with a complaint of dysmenorrhea, constant heavy dragging sensation in the pelvis, a loss of weight of from 10 to 15 pounds in the past eight months, and chronic constipation. This

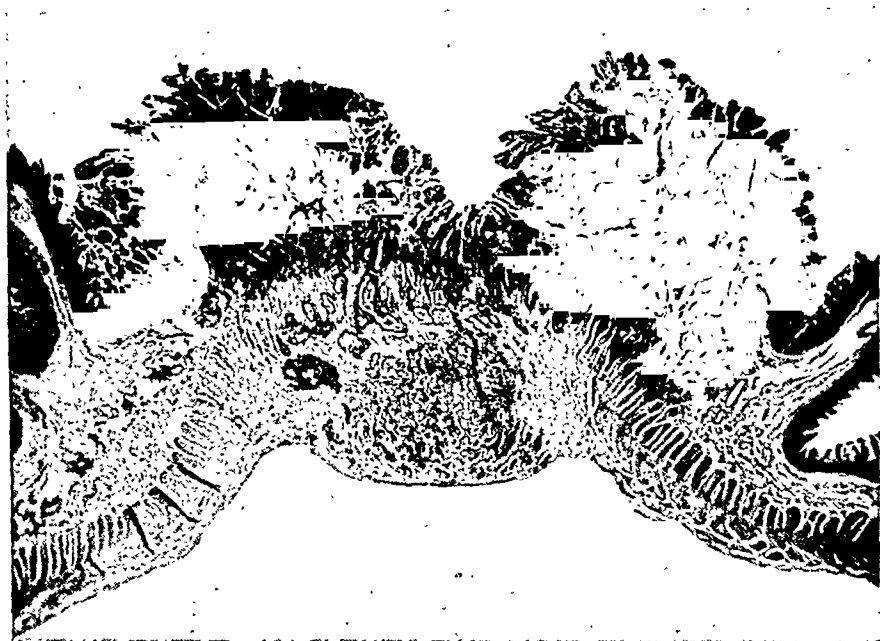


Fig. 1.—Low power microscopic view of the adenocarcinomatous lesion in the jejunum.

patient had been under medical supervision from time to time and had gained a few pounds in the past two months, but the dysmenorrhea had increased. She had had 4 living children, the youngest was three years of age, also one spontaneous miscarriage of about two and a half months' gestation, one year before the present illness. There was no pathologic gastrointestinal history of any sort other than the chronic constipation. The past history was irrelevant except that the 5 pregnancies had been close together and that the patient said she seemed progressively weaker with each pregnancy.

Pelvic examination showed the outlet relaxed, slight cystocele and rectocele. Cervix enlarged about two times, bilaterally lacerated, chronic cervicitis with eversion and erosion. The uterus was apparently anteflexed and pushed forward by a mass occupying the culdesac. The mass and uterus were freely movable together with the cervix as a single unit. The adnexa could not be palpated. The impression was of an ovarian cyst or myoma of uterus.

The patient was again seen some three weeks later after a very painful and

more profuse flow which lasted six days. The usual duration was four to five days.

Pelvic examination showed that the mass had now risen out of the culdesac. Together with the uterus it formed a nodular structure freely movable in the pelvis as a unit with the cervix. The tumor now reached to within about two fingers of the umbilicus. There was no free fluid in the abdomen, no marked tenderness or induration. Hospitalization for hysterectomy was recommended for the following week.

Five days later I was called to see the patient in her home because of severe upper abdominal pain, nausea, vomiting without a bowel movement for the past twenty-four hours. Abdomen distended and rigid; no palpable mass except the lower abdominal mass already described. Pulse was rapid and temperature normal.

The patient was hospitalized at once. After enemas the patient had several large bowel movements. All the nausea, abdominal distention, and rigidity dis-

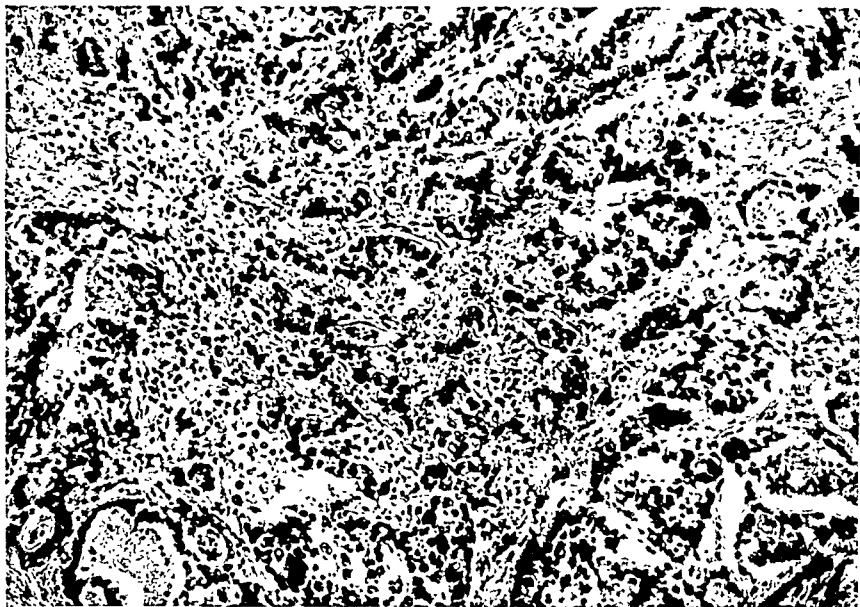


Fig. 2.—High power section through adenocarcinomatous lesion in the jejunum shown in Fig. 1.

appeared. The patient began to have vaginal bleeding with cramps although it was ten days before her expected menstruation.

A laparotomy was performed the following morning. The tumor mass was made up of a bilateral adenocarcinoma of the ovaries. The right ovary was about the size of a grapefruit, quite adherent to the uterus and several loops of ileum. The left ovary was only about one-half as large as the right and was also somewhat adherent to the uterus. The right ovary was mostly solid but contained a mass of necrotic hemorrhagic soft substance. The right ovary and tube were first removed with some difficulty because of the intestinal adhesions and the partial interligamentous nature of the tumor. Then the left tube and ovary together with the uterus and cervix were removed. The abdominal wall was closed with drainage. There was no free fluid or evidence of peritoneal metastasis.

The postoperative course was relatively uneventful for the first four days. Fluids were retained well. The bowels had moved and the patient had taken a soft diet. A blood transfusion had been given on the third day as a supportive measure. On the fifth day the patient suddenly began to have fecal vomiting and marked abdominal distention. Enemas were ineffectual, and the patient's temperature went

to 104° F. The condition grew steadily worse, large amounts of fecal vomiting continued. The abdomen remained soft but distended. The abdominal wound was clean and draining only a clear serosanguineous fluid. Clinically there was no evidence of peritonitis. The apparent intestinal obstruction continued. Under local anesthesia a rubber tube was placed into a loop of distended bowel and sutured with a triple purse string. Another blood transfusion was given. For a few hours the acute symptoms seemed relieved but the temperature went up to 107.5° F., and the patient died the following day.

Postmortem examination showed a low grade acute pelvic peritonitis without pus formation. A few small patches of fibrinous exudate were found on two loops of the ileum. When the jejunum was removed a crescent-shaped hard annular growth was noted in the wall of the bowel about ten inches below the duodenum. On section this proved to be a hard area of adenocarcinoma which had ulcerated into the lumen of the gut and was covered only externally by a thin layer of



Fig. 3.—High power microscopic section through a typical area as found in the right ovary.

peritoneum. There was no evidence of any other carcinoma. There was no metastasis. Several small mesentary lymph glands were sectioned without showing any carcinoma.

The microscopic sections from the jejunum and from the ovaries were strikingly similar. Both were adenocarcinoma of an intestinal type. The sections from the ovaries showed none of the Krukenberg pathology. The ovaries were solid tumors of a medullary adenocarcinoma type. The right ovary contained a large amount of necrotic, hemorrhagic brain-like substance but did not show cystic or papillary changes. The left ovary was mostly solid. The endometrium of the uterus showed no carcinoma. There was no carcinoma of the tubes. The cervix showed only a chronic cervicitis.

The following points should be summarized in conclusion:

1. Carcinoma of ovaries (bilateral) is so often secondary to some gastrointestinal cancer that every effort should be made to discover the latter before operation upon the pelvis is undertaken.

2. Krukenberg tumors are secondary to gastrointestinal carcinoma and are of a peculiar pathology; signet rings in a scirrhus carcinoma.

3. Other secondary types of ovarian cancer to gastrointestinal carcinoma should not be called Krukenberg tumors.

4. The unusual type of adenocarcinoma in the jejunum, recovered in both ovaries without change in type, emphasizes the secondary nature of these ovarian tumors.

This is verified by the fact that the endometrium, tubes, and cervix showed no carcinoma.

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3720 WASHINGTON BOULEVARD.

## PRIMARY CARCINOMA OF THE VAGINA FOLLOWING A BALDWIN RECONSTRUCTION OPERATION FOR CONGENITAL ABSENCE OF THE VAGINA

BY R. N. RITCHIE, M.D., ROCHESTER, N. Y.

(From the Department of Gynecology and Obstetrics, University of Rochester School of Medicine and Dentistry)

IN AUGUST, 1928, a young married woman, aged twenty-six years, presented herself to the Out-Patient Department of Gynecology of the Strong Memorial Hospital complaining of pain in the lower abdomen, discharge from vagina and rectum of three months' duration. Menstrual period normal in every respect. Previous health excellent. It was learned that she had been treated by her family physician for several months and had been told she had an abscess in the vagina which had been opened and drained several times. The last incision had been made into the rectum with the hope of promoting better drainage. All the above facts were obtained from the patient who was very cooperative and intelligent.

She was well nourished, of good stature, no loss of weight. Heart and lungs negative. No evidence of any palpable tumor mass. The scar of a midline incision was noted extending from the umbilicus to the symphysis, of which no mention was made in the history by the patient. Upon further questioning about the nature of the operation, all that could be obtained was that she had an operation at the age of twelve years and was very vague as to what had been done. This operative scar was disregarded for the moment with a hope of obtaining further data, as she gave us the name of the hospital at which the operation was performed and also the surgeon. Urine examination was negative. Blood picture was normal. Blood Wassermann was negative.

Pelvic examination at this time showed the vulva to be nulliparous and healthy. Urethra and Skene's tubules negative. Bartholin glands negative. No abnormal anatomic changes noted about the vulva, a point to be remembered on account of further data obtained at a later date. Vagina normal in size. About 2 cm. inside the fourchette was a mass the size of a large walnut, arising from the

posterior wall of the vagina, obliterating the lumen of the vagina to such an extent that it was difficult to admit an index finger above the mass without causing great pain and discomfort to the patient. For this reason it was impossible to examine the cervix, uterus, or appendages with any degree of accuracy.

The mass was friable, bled easily and showed macroscopic evidence of degenerative changes toward its center. It was tender and there was considerable induration on both sides along the lateral walls of the vagina. Pus could be expressed from the center of the mass, particularly with a finger in the rectum. Rectal examination showed the mass protruding into the lumen of the bowel but there did not seem to be any definite ulceration of the rectal mucosa, only a dimpling of the mucosa.

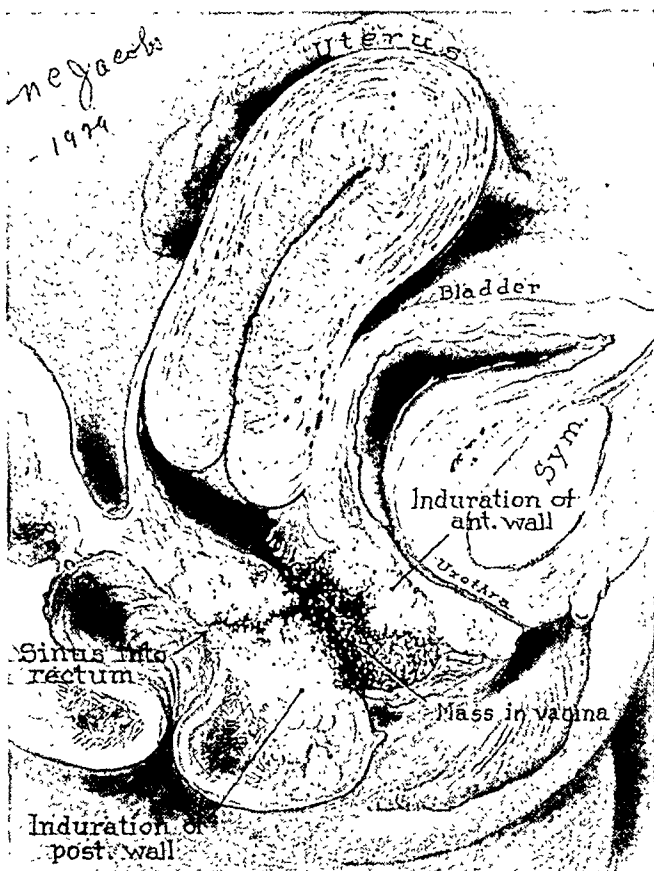


Fig. 1.—Diagrammatic drawing of the ulcerated mass in the vagina.

This apparently represented a sinus between the rectum and vagina which had been artificially made previous to promote better drainage.

Tentative diagnosis was made at this date of a malignancy of the vagina. The patient was admitted to the hospital for biopsy, proctoscopic examination, and further study.

After admission a more careful examination of the pelvis was made under anesthesia. Above the mass the vagina was normal. There seemed to be some shortening of the posterior fornix. The cervix was that of a normal nulliparous woman. The uterus was in good anterior position, normal in size, and freely movable. The appendages were normal. A biopsy was done at this time and serial sections were made.

After the diagnosis had been made, we were able to obtain more definite information concerning the midline scar below the umbilicus.

In November, 1913, at which date the patient was thirteen years old and attending school, she presented herself to Dr. Douglas Ward of the Rochester General

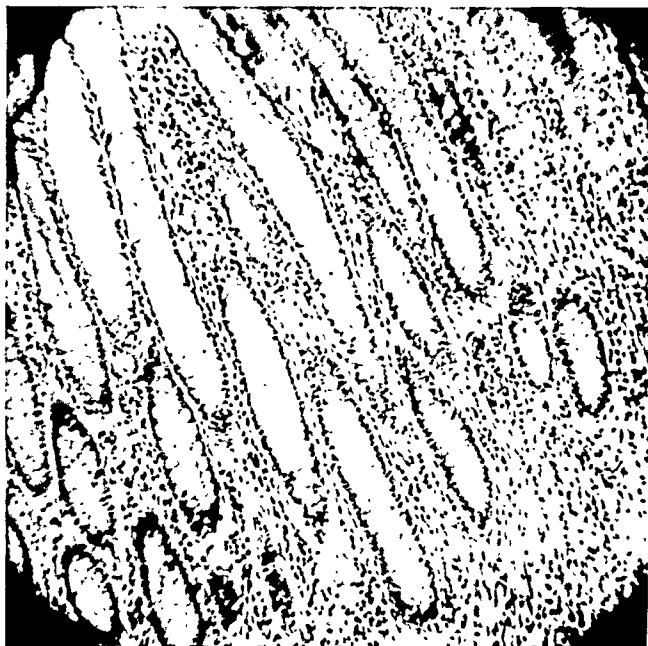


Fig. 2.—Showing characteristic goblet cells of the gastrointestinal tract. The presence of these cells was confusing as it was difficult to determine or explain their presence. Later information cleared the situation.

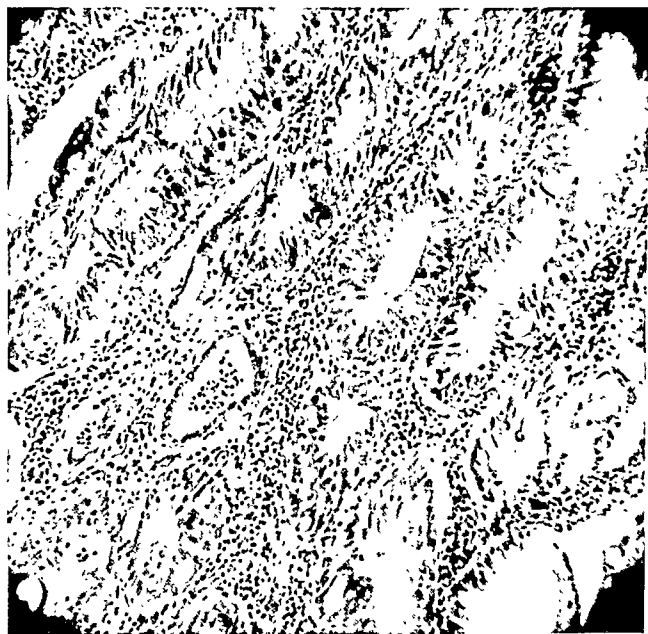


Fig. 3.—Shows definite adenocarcinoma.

Hospital with the following symptoms: Cramp-like pains in the lower abdomen, periodic attacks of vomiting and painful urination. These attacks gradually subsided and the patient was free from all symptoms. The same symptoms returned

again in five or six weeks, which suggested to Dr. Ward that these symptoms had some relationship to the periodicity and suggested some obstruction to the menstrual function, for up to this time she had never menstruated. At this time a vaginal examination was done and it was found that the patient had a congenital absence of the vagina.

She was admitted to the hospital February, 1913 and a résumé of the operation was as follows:

"A careful dissection was made between the bladder and rectum. At a depth of three inches from the incision of the mucous membrane, the cervix was reached. It was grasped with a tenaculum and pulled down, the connective tissue around it being pulled back until the external os of the cervix was exposed. A dilator was inserted into the cervix and about one ounce of black, tarry blood escaped from the uterus. The uterus and vaginal dissection were packed.

"Six days later an incision was made in the midline between the umbilicus and symphysis. A loop of small intestine twelve inches long, proximal to the cecum



Fig. 4.—Same condition as Fig. 3, considerable fibrous tissue formation.

was located. The loop was isolated from the rest of the intestine but was left attached to its own mesentery. The distal end of the loop was closed by a purse string suture of silk and half of a Murphy button was dropped into the short end of the ileum attached to the cecum. The other end of the loop was cleansed but not closed and the other half of the Murphy button was introduced into the proximal end of the ileum. The isolated loop was freed by making radiating incisions into the mesentery at each end to a depth of three inches, which allowed the loop to be pulled into the pelvis without cutting off its blood supply. Placing together the two halves of the Murphy button restored the continuity of the small intestine. The cut edges of the mesentery were sutured together, closing the gap in the mesentery and covering the raw edges.

"The peritoneum was opened into the cavity which had been made at the first operation and with a forceps, drew down the double loop of intestine to the vulva, stitching the opening around the cervix. Difficulty was experienced in placing sutures around the cervix and the open end of the bowel. The abdomen was



closed. The loop of intestine was opened at the vulva and the edges stitched to the surrounding tissue of the vulva (as previously stated, we were unable to note any defect at the vulva). Both ends of intestinal loop were packed with iodoform gauze. One year later the septum between the two loops of intestine was crushed."

This operation was performed as described by Baldwin, with a few personal deviations.

Following the operation the patient's menstrual function was normal, with no dysmenorrhea.

Six years later the patient married and her sexual history was normal, although she never became pregnant.

Dr. Ward stated at the end of his article, which was published in *Surgery, Gynecology and Obstetrics*, November, 1918, "The case is of unusual interest and the first case on record in which a vagina has been successfully made and connected with a functioning uterus so that regular menstrual function has been established."



Fig. 5.—High power, showing much the same arrangement as Figs. 3 and 4.

Dr. F. J. Baldwin, Columbus, Ohio, originator of the reconstructive operation for congenital absence of vagina, was given a résumé of the case. His reply was, "That he never heard of such a result from a physiologic or pathologic viewpoint. He could not see how there could be any malignancy except as it might arise in general principles, without regard to the operation."

The case is presented in the manner of coincidents, as we had to confront the problems which were hidden.

Our treatment was one of palliative measures. She was given three doses of radium, fifty milligrams varying in time from three to eight hours. The time elapsing between treatments was three weeks and deep x-ray therapy over the pelvis was given after radium treatments.

The patient's condition improved slightly for a time, but gradually the loss of weight, weakness and terrific pain after bowel movements increased. The generalized lower abdominal pain became more marked. The growth extended very rapidly and the greater part of the rectovaginal septum became involved. It was cartilaginous in character and had completely lost its elasticity. The tumor

extended along the lateral walls of the vagina and involved the anterior wall of the vagina and bladder.

December, 1928, five months after the first visit, the patient developed signs of an intestinal obstruction and a colostomy was done with the purpose of giving temporary relief. The pelvis was explored at this time and there was found to be a mass of carcinomatous metastases. The colostomy gave temporary relief for a short period. The patient died January 27, 1929, six months after her first visit to the hospital. Autopsy was refused.

We are unable to find any references in literature of a similar case.

### SUMMARY AND DISCUSSION

The history of a patient upon whom the Baldwin operation for the creation of an artificial vagina was performed thirteen years previously, is presented. Carcinoma subsequently developed in the newly created vagina. So far as I am aware, this is a unique occurrence. A number of interesting questions arise on which one may speculate, but concerning which no positive conclusions are possible.

Did the carcinoma develop as a result of the operation or would it have occurred had the bowel remained in its normal situation? It is obviously impossible to answer this, though one might make the comment that carcinoma of the small bowel is a very unusual pathologic lesion at this age.

Inasmuch as practically all of those women who present complete absence of the vagina usually present such defective development of the internal genitalia that menstruation is impossible, the question arises as to the nature of the original defect for which the Baldwin operation was performed. Was it a true absence of the vagina or did it represent a gynatresia acquired before puberty and resulting in occlusion of the vaginal tract with retention of the menstrual flow?

As this is the first example of its kind, one cannot fairly say that the Baldwin operation predisposes to malignancy.

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## SEX OF CHILDREN AFTER SINGLE OOPHORECTOMY

BY JOHN R. HARGER, M.D., CHICAGO, ILL.

THE question of sex determination as well as the cause of tubal pregnancy, make the following case history of more than passing interest.

Mrs. R. A. T., now aged forty-two, after having an ectopic pregnancy with rupture in 1915 gave birth to five boys.

Six weeks after rupture of a tubal pregnancy, the patient came under my care, when the right tube, ovary, appendix, a living functioning placenta with a large amount of liquor amnii were removed, together with a large, partially organized hematoma and a two months' embryo was taken from the culdesac. Each pregnancy, delivery and puerperium have been normal and without any unusual event other than after the fourth delivery; this child died on the fifth day from an undetermined cause. No postmortem permitted. Dates of deliveries were as follows: Aug. 1, 1915, Jan. 8, 1918, Oct. 28, 1920, Sept. 12, 1922, and Jan. 11, 1929.

A study of this case reveals several interesting points. The inflamed appendix adherent to the tubal mass after the ruptured ectopic may have been the cause of the tubal pregnancy. Five males from the left tube and ovary suggest the possibility of each ovary giving rise to separate sex. The father of these males is one of six boys born consecutively. His mother gave no history of pelvic pathology. The mother of these children had no brothers and only one sister. All of these males have shown a very marked resemblance, at the time of birth, to the maternal grandfather.

25 EAST WASHINGTON STREET.

# A STUDY OF VARIOUS LIVER FUNCTION TESTS IN NORMAL PREGNANCY\*

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THE liver is the largest, the most abused, the most neglected, one of the most important, and the least understood organ of the body. It has manifold functions, the most important of which has to do chiefly with the anabolism and catabolism of proteins. It also exercises a detoxifying action, making various noxious substances harmless by conjugation, splitting, or other processes. It stores carbohydrates in the form of glycogen, which it then changes to sugar and supplies to the body according to its requirements. It is concerned in some way with blood coagulation. It forms urea. Finally, it forms and secretes bile, which, in the presence of pancreatic juice, aids in fat absorption, plays a part in protein digestion, and stimulates peristalsis.<sup>7</sup>

As is well known, the liver suffers in many, and perhaps all, of the toxemic disturbances of pregnancy, especially those of the last trimester. Pathologic changes of a degenerative type are found,<sup>14</sup> and the majority of cases of acute yellow atrophy of the liver which have been reported occurred in pregnant women.<sup>72</sup> Even in normal pregnancy marked changes are frequently apparent, and it is claimed that the organ is enlarged and pushed upward in many healthy gravidæ. Mann and Higgins,<sup>44</sup> working with small laboratory animals, found that in pregnancy, especially near term, the emptying time of the gall bladder is decidedly increased; and, in their opinion, this fact suggests that in normal pregnancy some impairment of liver function always exists, even though it is not great enough to be demonstrated by any test as yet devised. A few workers with liver function tests, however, as will be noted below, report that some evidences of liver dysfunction in normal pregnancy are shown by a few of the tests employed.

It must be borne in mind, as Ray<sup>54</sup> points out in his study of liver function tests, that, unlike most other specialized organs of the body, the liver possesses a remarkable ability of regenerating and prolifer-

\*A digest of a thesis submitted to the Faculty of the Graduate School of Tulane University in partial fulfillment of the requirements for the degree of Master of Science in Obstetrics, April 1, 1928.

The majority of the tests on which this study is based were made in the laboratory of Touro Infirmary. The others were made in the biochemical laboratory of Tulane University, under the direction of Dr. Willey Denis. The preparation of the necessary reagents was done in Dr. Denis' laboratory and under her direction.

The scheme for the various tests and their application to the special patients were supervised by Dr. E. L. King, Professor of Obstetrics in the Graduate School of Tulane University.

The work herein reported was aided by a grant from the David Trautman Schwartz Research Fund of Tulane University.

ating in the face of the most profound insults. Experimenting with dogs, he found that as much as half of the liver substance could be destroyed by chloroform poisoning, and yet complete restoration would follow. He adds that these findings corroborate Roux's statement that the liver is the most silent of organs if only a moderate fraction of its cells are healthy. Ray also points out that since the functions of the liver are so various and since complete knowledge of them is still lacking, no one test is capable of measuring liver function as a whole; and all tests, therefore, must be interpreted with considerable caution.

Diamond<sup>16</sup> makes the same point, that since the liver is a complex laboratory with metabolic, excretory, and detoxicating functions, it is unreasonable to expect any one functional test to demonstrate the capacity of the liver as a whole. He believes that the only rational method is to utilize several of these tests on each patient, and this plan has been followed in this study. Diamond also points out that, inasmuch as four-fifths of the liver substance can be removed from an experimental animal and function still be preserved, it is well to remember that the human liver possesses the same ability, at least in some degree, and that no test can therefore be taken as an exact estimate of the amount of damage which has occurred.

The functions of the liver have been studied in many ways, and a large number of tests have been devised. Space does not permit of a consideration of them all, nor is it necessary to give the details of the various tests employed. Two dye tests are popular; in one, rose bengal is employed, according to the method developed by Delprat and his coworkers;<sup>15</sup> in the other, worked out by Rosenthal and his collaborators,<sup>58, 59, 60, 61</sup> phenoltetrachlorophthalein (and more recently bromsulphthalein) is employed. Intravenous injection of the dye is performed, and specimens of blood taken at stated intervals are examined for dye retention by colorimetric methods. Retention beyond the time ascertained to be normal is interpreted as evidence of liver damage. However, Ottenberg, Reuben and Abramson<sup>50</sup> and Rosenau<sup>56</sup> state that the use of the latter dye (phenoltetrachlorophthalein) is not free from danger, especially in the presence of an already damaged liver. Widal's hemoclastic crisis test, the van den Bergh, Fouchet, and icterus index test on the blood serum, the study of the sugar content of the blood and the urine after the ingestion of various sugars (especially levulose) by mouth, Schlesinger's test for excessive amounts of urobilin in the urine, and the employment of Ehrlich's aldehyde reaction for the detection of pathologic amounts of urobilinogen in the urine, appear to be the most popular and most useful of the various other tests that have been proposed.

A review of the literature shows that a majority of the studies on liver function deal almost exclusively with abnormal cases, and this is particularly true of work that has been done on pregnant women. Several papers have been published re-

porting investigations in toxemic patients, but only a few of these observers briefly mention their findings in normal pregnancy. Walthard<sup>74, 75</sup> states that in uncomplicated gestation there tends to be a hyperglycemia and an impairment of the storage ability of the liver, as well as an increase in the urobilin content of the urine. Graham,<sup>27</sup> writing of his experimental work with chloroform as a liver poison, states that somewhat similar changes occur during pregnancy, and especially in the last trimester, when, because of the demands of the fetus and placenta and because of the increase in the waste products to be detoxified, the maternal liver is subjected to a most unusual strain. P. F. Williams<sup>77</sup> subscribes to this view. Heyn and Messtorff<sup>31</sup> found the Widal hemoclastic test to be positive in one-third of a series of healthy women in the last month of pregnancy, and Couinaud and Clogne<sup>11</sup> report similar results. On the other hand, Strauss, working with levulose, found no evidence of liver dysfunction in normal pregnancy, so far as this test was concerned. As these reports are merely incidental, and as no detailed study of the response to the various liver function tests in normal pregnancy has so far been reported, it appeared to me that it would be worth while to conduct such an investigation for the purpose of determining whether these patients would show any deviation from the normal readings. It would seem that this work would be of value as a basis of comparison in studies of liver function in the toxemias of pregnancy.

I might mention at this juncture that studies on the function of the liver in the toxic states peculiar to pregnancy have been published by Walthard,<sup>75, 76</sup> Didier and Philippe,<sup>17</sup> P. F. Williams,<sup>77</sup> Smith,<sup>67</sup> Naujoks,<sup>49</sup> Krebs and Dieckmann<sup>37</sup>, Rosenfield and Schneiders,<sup>57</sup> Berkeley, Dodds and Walker,<sup>4</sup> King,<sup>35</sup> and Siegel.<sup>66</sup> Various tests were made by them, and it appears from a survey of their work that the dye test of Rosenthal (phenoltetrachlorphthalein and later bromsulphthalein) is of particular value, especially in the toxemias of late pregnancy, being generally found to be positive in a degree corresponding to the clinical condition. The van den Bergh test is as a rule positive in the severer cases of hyperemesis gravidarum, but is uniformly negative in the toxemias of the latter months. No report of the use of rose bengal in pregnancy was found in the literature. The other tests employed by these various authors appear to be of doubtful value.

In this investigation the following tests were used: the bromsulphthalein test, according to the technic of Rosenthal and White;<sup>60</sup> the levulose tolerance test, according to the method of Spence and Brett;<sup>68</sup> the hemoclastic crisis of Widal, as described by Gonzalez and Karr;<sup>26</sup> the van den Bergh test, according to the technic of the originator;<sup>71</sup> the Fouchet test, as described by Friedman and Straus;<sup>24</sup> the icterus index, according to the technic of Bernheim;<sup>5</sup> and the Ehrlich and Schlesinger tests, as described by Berkeley, Dodds, and Walker.<sup>4</sup> One hundred patients were studied, of whom sixty-one were entirely normal on gross examination, though naturally a minor pathologic condition, not sufficient to influence the pregnancy, was probably present in several of them. In all of these sixty-one patients the Wassermann reaction was negative, though this, of course, does not necessarily mean that they were free from luetic infection. Urinalysis, done routinely in each case, was normal throughout. For purposes of comparison, twenty-eight abnormal patients were studied, whose pregnancies were complicated by dental caries and pyorrhea, pyelitis, tonsillitis, syphilis,

or one of the various types of toxemia. Tests were also performed on eleven gynecologic patients as controls. A total of 1474 tests were made.

No patient was seen before the third month of pregnancy, and some did not report to the clinic until late in gestation. Specimens of blood and urine were obtained for the tests on the second visit, usually one week after the first, and the tests were repeated at monthly intervals until delivery. A few of the patients, who were admitted to the hospital, were studied during the labor and through the puerperium. Five patients in the normal group had not delivered at the completion of the study; but the pregnancies were progressing favorably, and uncomplicated deliveries were anticipated. Two of the patients in this same group were normal until the last month of pregnancy, when, during the last week, both exhibited symptoms of mild toxemia. In each instance this cleared up before delivery, and the puerperium was without incident.

In two of these cases specimens of blood were obtained from the cord at delivery and examined, with negative results, by the icterus index,

TABLE I

Normal pregnancy	61 cases
Abnormal pregnancy	28 "
Gynecologic	11 "

TABLE II

PATIENTS	WHITE	COLORED
Gynecologic (all sterile)	2	4
Primiparae	7	33
Multiparae	11	43
Multiparae with previous normal pregnancies	6	40
Multiparae with some previous abnormal pregnancies	1	7

TABLE III. TIME OF TESTS

From second trimester to labor	80
During parturition	6
10 days to 6 weeks postpartum	15
Gynecologic cases	11

TABLE IV. NUMBER OF TESTS MADE ON NORMAL PATIENTS

	1 TEST	2 TESTS	3 TESTS	4 TESTS	5 TESTS
Primiparae, white					1
Primiparae, colored	4	12	4	2	
Multiparae, white	4	1	1		
Multiparae, colored	14	7	7	2	2
Total	22	20	12	4	3

van den Bergh, and Fouchet tests. Four patients examined during labor showed a trace of bromsulphthalein retention, but all other tests made on them were negative.

In all of the normal patients studied during pregnancy the various tests employed gave uniformly negative results. This does not rule out the possibility of the occurrence of some degree of impairment of liver function; for, as stated above, it is generally agreed that there must be considerable damage before the tests will show positive readings. It is interesting to note that several of the patients had various incidental complications, which, according to the tests, occasioned demonstrable interference with the function of the liver. Thus, three patients with syphilis, inadequately treated before being seen, all gave a positive indirect van den Bergh reaction (nonobstructive jaundice); all had a trace of retention of bromsulphthalein, while in one patient the Fouchet test was slightly positive, and in one the icteric index was 10 (normal 4 to 8). In the fourth patient with syphilis, who had been thoroughly treated, all tests were negative while she was still pregnant. In 4 cases of severe pyorrhea complicating pregnancy, a trace of bromsulphthalein was found in each, and in one instance a positive indirect van den Bergh reaction. In the two patients that were retested three and four weeks postpartum, all tests were negative. In four patients with pyelitis there was dye retention in each (reaching 10 per cent in one case), a positive Schlesinger reaction twice, and a positive indirect van den Bergh reaction once. In those retested after proper treatment or after delivery, all tests were negative. In one patient with severe tonsillitis, there was 5 per cent retention of bromsulphthalein, while all the other tests were negative. The tests were not repeated postpartum. In a case of mitral regurgitation with insufficiency there was a trace of bromsulphthalein retention at the eighth month, with 5 per cent retention during delivery; the indirect van den Bergh test was positive both times. All tests were negative postpartum.

These findings would appear to indicate that the usual wide "margin of safety" is much reduced, for certainly such conditions would hardly affect perfectly normal livers to any appreciable extent. The fact that four patients tested during labor showed a slight retention of bromsulphthalein would point to the same conclusion.

The tests performed on the thirteen patients with toxemias bear out the results previously reported by others. There were four cases of nephritic toxemia, three of severe preeclamptic toxemia, one of eclampsia, and five of mild preeclamptic toxemia. The various tests were positive in differing degrees, the most reliable one being the bromsulphthalein test, which was positive in ten instances, the percentage of retention corresponding fairly well with the clinical picture.

## SUMMARY AND CONCLUSIONS

I have pointed out that even in a normal pregnancy, because of the increased demands on the maternal organism, the physiologic processes of the liver are subjected to extra stress. The strain grows more intense as pregnancy advances and is naturally greatest during the last trimester and particularly during labor. Shortly thereafter there is a return to normal conditions. In spite of this added strain, the average liver, beginning its ordeal with no pathologic condition, will function well. On the other hand, a liver already damaged or unfit for this extra task, or a liver involved in pathologic conditions peculiar to pregnancy, will promptly give evidence of dysfunction. Any tests, therefore, which will demonstrate this dysfunction and which, particularly, will demonstrate it promptly, are extremely valuable.

No one test is sufficient to demonstrate liver dysfunction, because of the manifold duties which this organ is called upon to perform. On the other hand, a positive result in any test undoubtedly means that impaired function of some sort is present, even if it is not apparent clinically, and that patient should be observed with special care in order to forestall possible trouble and to detect it immediately when it occurs. It is fair to conclude from the tests performed in this study that, other things being equal, the average liver is entirely capable of withstanding the added strain of pregnancy.

Patients with coincident disease, not of obstetric origin, need very careful watching. Patients with luetic infection, if properly treated, may carry the child to term and deliver spontaneously; but liver damage may result, as was evident in the cases in this series. Pyelitis, tonsillitis, and similar infections which cause a rise in body temperature place an added strain on the liver if the results of these tests are to be accepted, and such patients should be watched from that point of view also.

While this study was undertaken primarily with the idea of studying the liver of normal pregnancy, the abnormal cases give grounds for comparison, and the entire investigation warrants the following conclusions:

1. The bromsulphthalein test is probably the most helpful of all. It is invariably negative in normal cases; but if any retention is shown, complications are to be looked for. It can be employed with impunity, for it seems to produce no ill effects on the patient, immediate or remote.

2. The van den Bergh test is valuable only in occasional cases.

3. The icteric index test is valuable in that positive results point to hepatic insufficiency.

4. The Fouchet, Schlesinger, Ehrlich, levulose tolerance, and Widal hemoclastic crisis tests are not uniformly reliable.



5. All tests, even those whose reliability has been established, should be interpreted with caution, because of the fact that no one test can demonstrate the functional ability or disability of an organ with manifold functions.

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## THE BLOOD TEST FOR OVARIAN HORMONE\*

### SECOND REPORT

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(From the Evans Memorial)

MANY years ago clinical observations demonstrated that the ovary, with its secretion, is the controlling factor in the functional maintenance of the female genital tract. Physiologic experimentation and the clinical use of preparations of the whole ovary or its fractions have proved the presence of an internal secretion. There is, moreover, evidence tending to show the presence of more than one. In spite of these steps forward in the laboratory, and of some rather glowing reports of the results of clinical administration of ovarian preparations, the clinician has been no further advanced in the diagnosis of the functional condition of the ovary.

In 1915 Frank<sup>1</sup> and his coworkers reported the occurrence and extraction of physiologically active substances in the corpus luteum and the placenta. In 1922 a substance with similar reactions was demonstrated in the fluid of the graafian follicle.<sup>2</sup> In 1925<sup>3</sup> the same investigators reported the presence of similar substances in the circulating blood, and in the following year they elaborated a test<sup>4</sup> for ovarian activity, based on the clinical variations of the blood content of the active substance, corresponding to certain phases in the menstrual cycle.

The elaboration of such a direct test of ovarian functional activity was of importance particularly from two points of view. In the first place, it offered a clinical method of potential value in the diagnosis of patients with menstrual aberrations and ovarian disease. Secondly, it offered a means of studying the functional activity of the ovary in patients suffering from abnormalities of other glands of the endocrine series.

\*Read before the Annual Clinical Session, American College of Physicians, April, 1929.

In view of the important potentialities of the test, repetition of the work was undertaken almost two years ago. The results in a series of nonpregnant women have been reported<sup>5</sup> elsewhere, and the present communication deals with the findings in a series of postpartum cases. In each series, bloods from pregnant patients were used for controls, and the combination of these two series of pregnant bloods more than doubles the group reported as controls in the previous paper.

#### METHODS

The technic of the test as here used varies somewhat from that described by Frank. These differences have already been described and the reasons for the changes discussed, so a concise description of the several steps will suffice here.

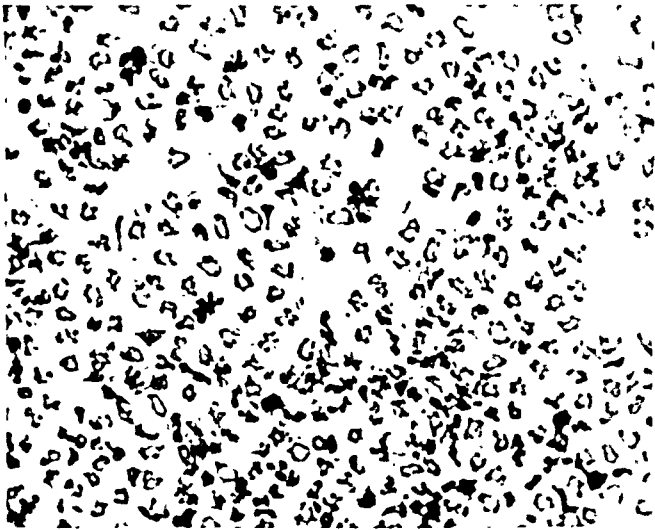


Fig. 1.—Diestrous smear, composed entirely of leucocytes.

*Collection and Extraction of Blood.*—Forty cubic centimeters of blood from the arm vein are put directly into a Petri dish containing 50 or more grams of pulverized anhydrous sodium sulphate. The blood and sulphate are mixed with a spatula until they form a dry crumbly mass. This mass is put into a mortar and repulverized. The resulting powder is extracted in an Erlenmeyer flask with several fractions of ethyl ether, which together total not less than 175 c.c. Rough separation of each fraction from the blood sulphate mixture is made by decantation. All of the ether fractions are finally combined and sedimented in a centrifuge. The solid portions which have come over in the rough decantations are thrown down into a relatively compact cake, and clean decantation from this is easy. The resultant extract should be a clear, slightly yellow solution. This portion is put into a shallow dish and evaporated to dryness. The yellow lipoid material remaining is emulsified with 2 c.c. of sterile water, or is taken up in like quantity of oil of sesame. The extract is then bottled and stoppered and is ready for injection. All steps in the preparation of the extract after the evaporation of the ether fractions must be carried out under aseptic technic.

*Castration of Mice.*—The indicator for the test is the castrated female mouse. The work of Stockard and Papanicolaou<sup>6</sup> on guinea pigs, Long and Evans<sup>7</sup> on rats,

and Allen<sup>8</sup> on mice, has shown that there is a definite cytologic change in the vaginal smears of these animals at different stages of the estrous cycle, and that these changes may be used to fix the phase of the cycle in which the smear is made. (Figs. 1 to 4 represent the typical appearance of vaginal smears at different stages of the cycle.) These same investigators have proved that after castration the vaginal smear takes on the characteristics of the diestrous stage of the cycle and maintains them continuously. However, if ovarian tissue be transplanted into the castrated mouse, or if the mouse be injected with some active ovarian preparation, an artificial estrous cycle results. During this cycle the vaginal smears show all the changes characteristic of the normal cycle. This reaction of the castrated mouse to active ovarian material forms the basis of the test.

The castration of the mice is difficult only because of their size. As soon as the operator becomes accustomed to the small tissues and the delicacy required in handling them, the operation offers no technical difficulties. The mice are very resistant to infection and only the minimum of aseptic precaution is required.

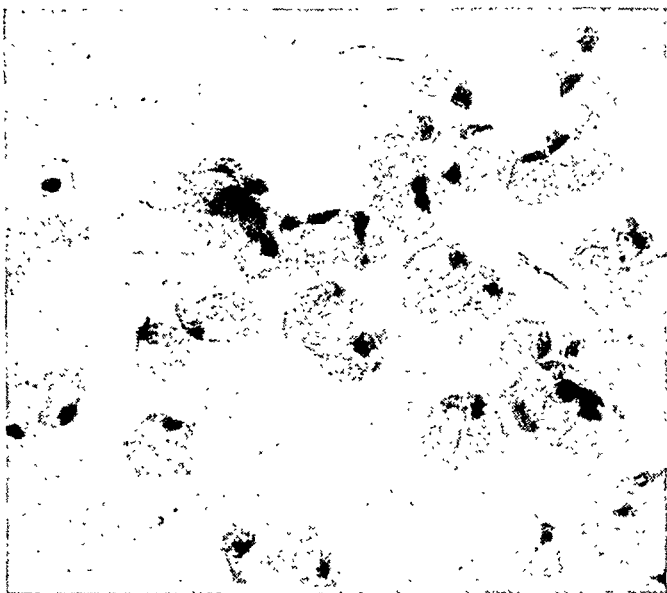


Fig. 2.—Early proestrous smear, showing large numbers of nucleated epithelial cells, small and sharply staining.

Instruments and towels are sterilized and the hands are washed and rinsed with alcohol. The skin of the mouse is disinfected with half-strength tincture of iodine. We have found it unnecessary to shave the skin, and have discontinued the use of depilatories as too irritating. There are two approaches to the ovaries: abdominal and dorsal. We have always used the former in mice, although the latter has been very satisfactory with rats. The abdominal route was chosen because the injections are made under the skin of the back, and it was felt that the operative scar would render them more difficult. The incision is made in the midline of the abdomen, extending well down to the pubes. At the lower end of the incision within the peritoneal cavity will be found a tab of omental fat. Behind this and attached to it is the bifurcation of the uterus. One of the cornua is followed upward to the kidney region, where the cornu ends in the fallopian tubes. This is tremendously convoluted and is in intimate association with the ovary. The mesentery, which attaches the tube and ovary to the lower pole of the kidney, is grasped in a pair of forceps and pulled loose. The ovary, tube, and end of the uterine cornu are then severed. No ligature is necessary unless the mouse is in

estrus and the organs are very much congested. The same procedure is carried out on the other side. The abdomen is then closed in two layers with fine silk. The wound is touched with iodine and covered with collodion. It is important to imbed the stitches in collodion; otherwise the mice bite the stitches and loosen them.

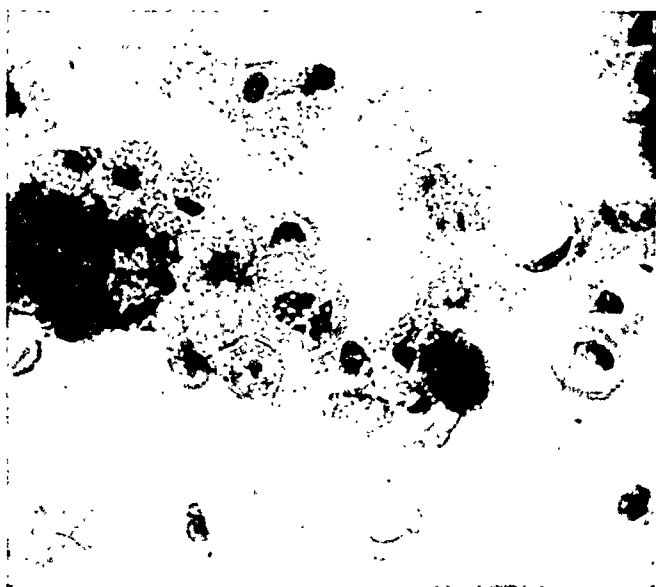


Fig. 3.—Late proestrus, nucleated and cornified epithelial cells. The former are swollen, faintly staining and are evidently devitalized.

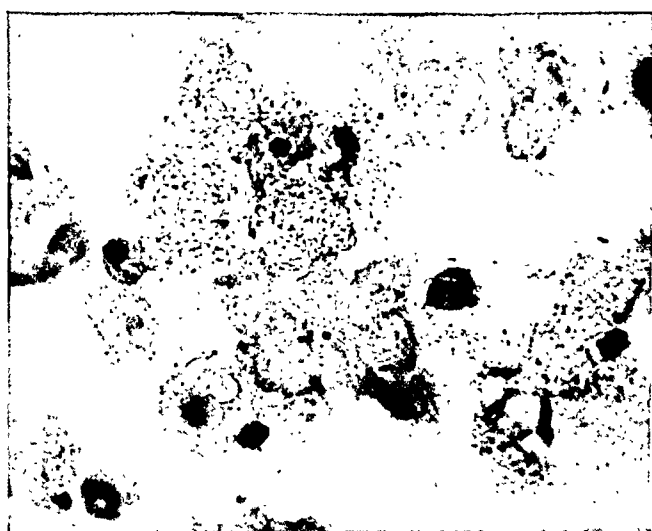


Fig. 4.—Estrus, smear composed almost entirely of cornified cells with rare nucleated cells.

The mortality of the operation is very low, and most of the deaths are due to the anesthetic. The stitches are not removed. Recovery is rapid and the mice are ready for use after a week.

*Injectiions.*—The injection of the test materials is made under the skin of the back. The total dose is given in three fractions at intervals of about three hours. During the first series, the extracts were all used in the form of emulsions in

sterile water, with a small amount of sodium carbonate added in some cases to aid in the emulsification. In the present series most of the material has been injected in oil of sesame. This has been used by many observers, and from their reports and our own experience the results are the same as with the emulsions. In one respect the oil is more satisfactory. There are fewer skin sloughs following its use than after the emulsions.

*Smears.*—All the animals have control smears made on the two days preceding injection and on the morning of the test, to preclude the possibility of spontaneous ovarian activity. Several observers have reported regeneration of ovarian tissue after castration. Test smears are taken on the morning and evening of the two days succeeding the injection and on the morning of the third day. The smears are air-dried and stained with one per cent aqueous solution of thionin. No fixation is necessary though it does no harm. The readings are made according to the scale used by Frank in his work, as no adequate basis for comparison would be obtained otherwise. On this basis, a smear composed mostly of epithelial cells

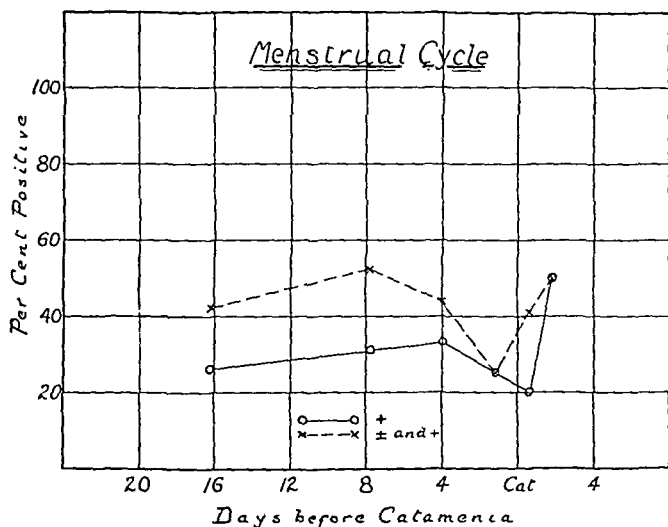


Fig. 5.

would be classed as two-plus, or weak positive; a smear composed only of nucleated and cornified epithelial cells would be numbered three and called threshold; and one composed entirely of cornified cells is numbered four and called strongly positive.

The results previously reported show considerable variation from those published by Frank.<sup>9</sup> They are shown in Fig. 5 and Table I. Comparison of these figures with those of Frank shows that the trend of the curve is opposed in the two series, and this divergence is most marked in the premenstrual period of the cycle. The obvious criticism would be that some of the changes in the preparation of the blood extracts have made the difference. Such an error, however, would cause either false positives or false negatives, whereas the curve shows a higher number of positives than Frank in the intermenstrual interval, and a lower number in the premenstrual stage. A condition of this kind cannot arise from a single error. In order to show that this

divergence is not the result of too rigid a standard in reading the smears, a second curve has been drawn, which combines the tests which were doubtful with the positive ones. It will be seen that this increases the disparity rather than the reverse. Furthermore, in the premenstrual portion of the cycle, which is the most important part, the addition of the doubtful tests does not change the curve, as at this time the tests gave clear-cut positive or negative results. It is realized, of course, that neither of these series is large enough to be conclusive.

TABLE I. MENSTRUAL CYCLE

DAYS BEFORE CATAMENIA	10-	10-6	5-4	3-1	FIRST DAY CATAMENIA	SECOND DAY CATAMENIA
Number	24	7	5	4	1	1
Per cent	26	30	31	25	20	50
Number	15	5	2	0	1	0
Per cent	16	22	13	0	20	0
Number	55	11	9	12	3	1
Per cent	58	48	56	75	60	50
Totals	94	23	16	16	5	2

During the past six months we have collected data on the disappearance of the active substance from the blood of postpartum patients. The technic of the test has been the same as that described above. The test was controlled by including one or more specimens from pregnant patients in each group of tests. It has been suggested somewhere that the mechanism of the onset of labor might be connected with the dis-

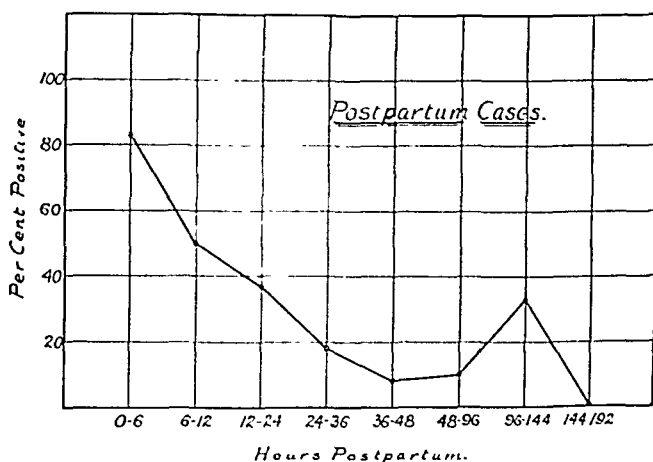


Fig. 6.

appearance of the active substance from the blood. In order to test this suggestion, many of the antepartum bloods in this series were taken during the course of labor or as nearly as possible before its onset. All of these bloods gave positive reactions, and we may assume therefore that the onset of labor does not depend on a disappearance

of the hormone from the blood. This agrees with the findings of Smith,<sup>10</sup> who reported that the concentration of the hormone was greatest just before labor.

The tests on postpartum cases show that there is a rapid and progressive disappearance of the active substance from the blood after delivery of the patient. This applies to the unit dose of 40 c.c. of blood which was used throughout the experiment. The curve of positives plotted in Fig. 6 shows a slight rise in the forty-eight to ninety-six hour period, and in the ninety-six to one hundred and forty-four hour period over the results shown in the thirty-six to forty-eight hour group. I am convinced that these first two are too high, the error being due to the small number of tests involved in each group. The regularity of the curve, with these two exceptions, makes this probable.

TABLE II. POSTPARTUM CASES

HOURS POSTPARTUM	0-6	6-12	12-24	24-36	36-48	48-96	96-144	144-192
Number	5	1	3	4	2	1	2	0
Per cent	83	50	37	18	8	10	33	0
Number	1	1	2	3	4	0	0	0
Per cent	16	50	25	13	16	0	0	0
Number	0	0	3	15	19	9	4	3
Per cent	0	0	37	68	75	90	66	100
Totals	6	2	8	22	25	10	6	3

Although the difference in method is great enough to make comparison difficult, there seems to be no conflict between these figures and those reported by Smith on postpartum bloods. The two positive results which she gives would naturally fall into the positive area of Table II if made to conform to the unit dose of 40 c.c. as here used. Of the several negative results which she reports, some would fall into the negative area of the table and the remainder cannot be allocated because of difference in method. Table II gives the numbers and percentages of the positive, doubtful, and negative tests in the present series.

It must be noted here that this series is unselected. These figures represent the total of all tests performed with the exception of one case where only one-half the dose of blood was obtained. This test was negative and had to be thrown out because there was no way to judge if the result were truly negative or due to the decreased dosage of blood. On the other hand, two tests in which the amount of blood was 30 and 35 c.c. respectively are included in the series. Both were doubtful results but they were included because they furnished evidence of activity.

The following group of pregnant cases is also unselected. The group



from the previous paper has been taken over as originally reported and there are no deductions made among the new group of cases which has been added. Table III and Fig. 7 show the results in this group. Here again the figures given under the fifth and sixth lunar months are probably distortions due to the small numbers involved. Assuming this to be true, the curve confirms in a general way the results reported by Frank, although he shows a higher percentage of positives in the early months of pregnancy.

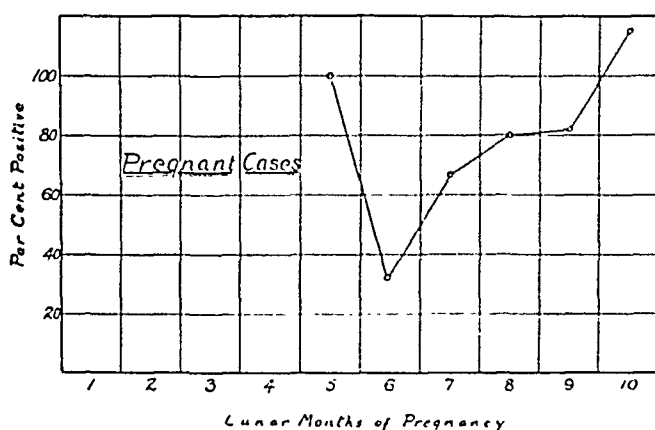


Fig. 7.

TABLE III. PREGNANT CASES

LUNAR MONTH OF PREGNANCY	2	3	4	5	6	7	8	9	10
Number				2	1	6	5	14	39
Per cent				100	33	66	83	82	95
Number				0	1	3	1	3	0
Per cent				0	33	33	16	18	0
Number				0	1	0	0	0	2
Per cent				0	33	0	0	0	5
Totals				2	3	9	6	17	41

## CONCLUSIONS

In a series of blood tests performed on postpartum cases, the estrus-producing substance was found to disappear rapidly after delivery from the circulating blood of the patient. This applies to the dose of hormone contained in 40 c.c. of blood.

In a series of tests performed by the same method on pregnant patients, which included 36 cases previously reported, the proportion of positive tests increased with the duration of pregnancy until it reached 95 per cent in the tenth lunar month.

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252 MARLBOROUGH STREET.

## PUERPERAL INVERSION OF THE UTERUS. CLASSIFICATION FOR TREATMENT

By FOSTER S. KELLOGG, M.D., BOSTON, MASS.

BY PUERPERAL inversion of the uterus is meant inversion of the normal uterus subsequent to the birth of the child. Cases of inversion of the uterus complicated by uterine tumors doubtless present a different problem and are not considered here. We are concerned only with classification for treatment.

Puerperal inversion of the uterus is statistically very rare. Williams quotes St. Petersburg and Dublin statistics. We suspect the Russian uterus has better muscle tone than the American, and we are sure that the conduct of the third stage is more carefully carried out in Dublin than in Boston. Several of us together have observed 7 cases (5 of which have been reported together) in the last few years in and about this city and I doubt in this time if together we have seen 250,000 labors or 193,833 deliveries. These figures are given in the above cities without the appearance of a single case. Williams says the diagnosis is easy, and we agree that it should be, but in our experience we have seen it overlooked by well-trained obstetricians. The fact that chronic cases turn up for operation from time to time suggests also that some cases are missed when acute. A study of death certificates in the puerperal state in Massachusetts for the last three years leads me to feel that an occasional case set down as a death from postpartum hemorrhage was an inversion death. This is of course purely a matter of opinion. However, these facts lead to the belief that inversion of the uterus is not so uncommon hereabouts and that proper treatment of the condition warrants this article.

A perusal of the subject in latest editions of excellent textbooks of gynecology and obstetrics (Graves and Williams for example) shows that puerperal inversion falls between the two, the one passing the subject to the other. That it is inadequately covered by both is apparent to anyone who has got up against his first case in consultation some hours after the inversion, and seeking information as to treatment from the books, follows it.

Textbooks classify this condition as acute and chronic. For acute inversion immediate reposition from below is advised. For chronic in-

version a cutting operation on the cervix from below of the Spinelli type is advised. So far as this classification and treatment go one must agree with it. Unfortunately, for practical purposes this textbook classification omits one variety of the condition which is certainly not yet "chronic" and yet is not quite "acute." This is perhaps the most common variety seen, always in consultation practice. As everybody knows and as textbooks sometimes stress, at some time after the inversion the cervical ring tightens. How soon this takes place I do not know but I have reasons to believe that it may occur in a very short time. Following this phenomenon, according to textbook classification, the case is still acute and dilatation of the ring and reposition of the inverted uterus from below are advised. That this can sometimes be done with a patient still alive is probably undeniable. But that this effort probably accounts in a large measure for the high mortality in the condition no one could doubt who has tried it. This procedure is like chasing a greased pig in a poke. While one attempts it to his own manual exhaustion, the patient is prone to bleed freely, usually having bled a great plenty already, and drifts rapidly into a condition of profound shock and hemorrhage. This wholly because of the manual difficulty of replacing the large edematous fundus back through a ring which will not stay dilated, all with a single hand. By the same token, to think of doing a Spinelli type operation at this time in the face of the blood oozing and distorted tissues is to conceive of a very shocking and bloody operation.

As long ago as 1921 (ample time for textbooks to take recognition of it), Huntington<sup>1</sup> devised the operation of abdominal replacement of the inverted uterus. In 1928 Huntington, Irving and Kellogg<sup>2</sup> described the technic with illustrations and reported 5 cases successfully operated upon by this method.

Shock primarily (as a careful perusal of reference<sup>2</sup> will show) and hemorrhage secondarily are the immediate dangers of inversion of the uterus. As has been stressed by others it is axiomatic that a successful treatment of any obstetric complication which has already resulted in hemorrhage and shock, as for example, placenta increta, placenta previa and ablatio placentae, depends on the complete prevention of further hemorrhage and shock. The gentle simplicity of the Huntington technic meets this requirement in inversion of the uterus after cervical contraction both in theory and in practice, attempts at replacement from below, certainly do not meet it.

Two other remote risks that I would call to your attention are: sepsis from the exposed, often packed uterus, and reinversion. As a guard against the first, should one sometimes do a supracervical hysterectomy after the reinversion? As a guard against the second should a light suspension suture be fixed through the fundus? Experience does not

permit me to answer these questions but they must be borne in mind in any future consideration of the subject.

#### CONCLUSION

The statements made above I believe permit us to offer the following reclassification of puerperal inversion of the uterus each with its appended appropriate treatment:

*Acute Inversion.*—Discovered before cervical ring formation. Immediate manual replacement from below.

*Subacute Inversion.*—Discovered after cervical ring formation. Abdominal replacement Huntington technic.

*Chronic Inversion.*—Spinelli type cervix spitting operation from below.

Whether one obstetrician prefers to examine for ring formation if an interval has elapsed since inversion occurred probably matters little if done under aseptic conditions, and he stops there if the ring has formed. Personally unless the inversion occurred in a patient I had just delivered myself I would rather assume the cervical ring already present and replace abdominally.

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19 BAY STATE ROAD.

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**Keiffer:** Torsion of the Gravid Uterus. Bruxelles-med. 7: 314, 1926.

A multipara, aged forty-four, had had six years previously a Baldy-Dartegnes operation for retroversion. During the fifth month of the existing pregnancy the patient suffered a severe attack of enteritis, diagnosed as intestinal grippe. From the seventh month on she developed repeated small uterine hemorrhages, with increasing edema of the left leg, thigh, and vulva and of the cervix. The patient went into labor at term, the fetus being in the transverse position. A marked inclination of the uterus to the right was noted. Because after five hours of intensive labor no cervical dilatation had occurred, and in view of the edema, transverse position and probability of a low implantation of the placenta, a cesarean section was decided upon. Upon opening the abdomen the uterus was found densely adherent to the surrounding viscera and rotated on the cervix from left to right so that the uterine incision had to be made on the left side of the fundus parallel to the broad ligament. A living child was delivered, the placenta extracted and the incision closed without trouble. The patient made an afebrile and uninterrupted convalescence.

Keiffer feels certain that it was the operation followed six years later by the intestinal infection with adhesions that produced the uterine torsion.

THEODORE W. ADAMS.

# PREMATURE SEPARATION OF THE NORMALLY IMPLANTED PLACENTA

## AN ANALYSIS OF 61 CASES

BY R. A. BARTHOLOMEW, M.D., ATLANTA, GA.

*(From the Department of Obstetrics, Emory University Medical School)*

**B**Y DEGREES, rational conservatism, in its application to the treatment of obstetric complications, is gaining recognition. Such, however, has not been the attitude toward premature separation of the normally implanted placenta. There exists an all-too-prevalent feeling that forcible delivery, operative or otherwise, is strongly indicated, especially in the severe type of this condition. It was with the express purpose of comparing the results of conservative and radical treatment, that a study of this series of cases was undertaken, as well as a review of some outstanding reports in the literature.

Over a period of ten years, from September, 1918, to September, 1928, the records of the colored maternity service of Grady Hospital showed 61 cases of premature separation of the placenta, in a total of 9,208 labors, approximately one in 150 labors. Fifteen cases were of the severe type, as manifested by shock and anemia, 7 were moderately severe, and 39 were of the mild type.

Twenty-nine cases occurred in patients from fifteen to twenty-four years of age; 27 cases in patients from twenty-five to thirty-four years of age, and 5 cases in patients from thirty-five to forty-four years of age. There were 18 primiparae and 43 multiparae. Thirty-six cases occurred during the ninth month, 15 during the eighth, and 10 during the seventh month. The Wassermann reaction was negative in 43 cases and positive in 6 cases, a frequency of 14 per cent, or approximately the same as that of the general service at the present time.

Toxemia, as indicated by albuminuria, hypertension or previous toxic symptoms, was found in 33 cases, or more than half of the entire number. In 2 patients, a short cord; in 1, unruptured membranes; in 1, hydramnios; and in 1, trauma appeared to be the etiologic factor. In 23 cases there was no apparent cause, but in 6 of these patients a condition of shock produced a low blood pressure and there was no record of a urine examination. It is probable that some of these were associated with toxemia. There were 5 cases of twins in the series, this being over five times the normal proportion. There were no cases of eclampsia.

The hemorrhage was external in 56 patients and concealed in 5 patients. Definite tenderness and rigidity of the uterus were found in 38

patients, including all the serious cases; in 2 patients the uterine muscle was apparently soft. In the remaining 21 patients, no note was made of this important finding. Whenever possible, a vaginal examination was made to eliminate the possibility of placenta previa. More or less severe shock was present in 17 patients. The placenta showed the typical appearance of premature separation in 52 patients; in the remaining cases the placenta was not adequately described but clinically the diagnosis was certain. Due to a more or less complete separation, the placenta was expelled spontaneously at once or very soon after the birth of the child in 19 cases.

The treatment is classified as follows: (1) watchful expectancy which includes one or more of such measures as rupture of the membranes, the use of an abdominal binder, pituitrin, ergot, morphine, subcutaneous or intravenous glucose or saline solution to combat shock, and transfusion for anemia; (2) conservative interference which includes the use of the dilating bag or catheter to induce labor, or low forceps or breech extraction to hasten delivery; (3) accouchement forcé which includes manual dilatation of the cervix, internal version and extraction or difficult forcep delivery and, (4) cesarean section with or without hysterectomy or vaginal hysterotomy.

Fifty-two patients, including 6 severe or moderately severe patients, were treated by watchful expectancy with only one death, which occurred on the seventh day, due to antepartum infection manifest on admission and not attributable to the manner of treatment.

Five patients, including 4 of the severe type were treated conservatively, labor being induced with a bag. There were 3 deaths in this group. In 1 patient, death occurred three hours after delivery, apparently from shock and hemorrhage, the latter being of the concealed type during the second stage and continuing after the third stage, although the uterus was packed. In another patient, death occurred one hour after delivery by forceps, during which a third degree laceration was sustained, and immediately following which a severe degree of shock developed. The excessive trauma of the forcep delivery undoubtedly produced a fatal degree of shock, as the hemorrhage was not excessive. Definite evidence of toxemia was present in both of these cases. The third death in this group occurred from shock and hemorrhage five hours after admission. The patient had a fibroid uterus and died undelivered. A suitable donor for transfusion could not be found. The membranes were ruptured artificially and labor induced by the bag method. Autopsy showed the placenta to be almost completely detached, and the hemorrhage concealed.

Three patients, one of whom was of the severe type, were delivered by internal version and extraction and all recovered, although in one patient prompt stimulation for shock was necessary immediately after delivery.

One patient, of the severe type was delivered by cesarean section and the uterus removed. She made a good recovery although the baby was stillborn.

The total maternal mortality was 6.5 per cent. Excluding the death due to antepartum infection, the mortality was 4.9 per cent.

There were 39 stillborn babies. Ten of these were more or less macerated. Twelve babies died after delivery, the majority within a few hours. The total fetal mortality was 83.5 per cent. On account of the extremely high fetal mortality associated with premature separation of the placenta, the choice of treatment need not be influenced to any great extent by a consideration of the child's welfare.

The sudden onset of abdominal pain and hemorrhage in the last trimester of pregnancy usually indicates premature separation of the normally implanted placenta, but the diagnosis and treatment call for thoroughness in the examination, good judgment and care to avoid any procedure which may aggravate or give rise to shock.

The history generally gives indication of preexisting toxemia, manifested by previous headache and swelling. The onset is usually acute with moderate bleeding and more or less severe abdominal pain, not well localized. There is continuous discomfort, increased at intervals, if labor has begun. The patient may complain of faintness or extreme weakness and shortness of breath if shock or hemorrhage is at all marked.

The examination should first be directed to an estimate of the patient's general condition as shown by the general appearance, color, temperature, pulse, respiration, and blood pressure. The latter may be very low if shock is present or the loss of blood excessive. A blood count should be made, the hemoglobin estimated and a specimen of blood taken, to be matched and typed for transfusion should the latter be necessary. On abdominal examination, note should be taken of persistent tenderness and rigidity, which are usually so marked that fetal outlines and fetal heart sounds are difficult to obtain; also, of the occurrence of regular contractions, indicating that labor is in progress. Finally, a vaginal examination is made to eliminate the possibility of placenta previa, being prepared at the same time to obtain a catheterized specimen of urine and to rupture the membranes or insert a dilating bag if indicated. The bleeding is usually observed to be of a darker color than that associated with placenta previa.

Conclusive evidence of premature separation is found in the appearance of the placenta after delivery. It almost invariably shows a much darker bluish appearance and adherent black clots over the area of detachment. The placenta often follows the delivery of the child at once or after a very short interval, due to previous more or less complete separation, and is accompanied by a number of tough, black clots.

There are fundamental differences between placenta previa and pre-

mature separation of the placenta in regard to the general condition of the patient and the nature of the bleeding. These basic differences must be the guide in choosing a rational treatment.

The severe type of premature separation is usually complicated by a toxemia which is apparently of a different nature than that of pre-eclamptic toxemia. The toxic element appears to have a destructive effect on the delicate walls of the smallest blood vessels, which is apparently the direct cause of the hemorrhage at the placental site and, in some cases, of hemorrhages elsewhere. Several patients in this series vomited considerable dark blood during labor. This also accounts for the fact that occasionally there is an extravasation of blood between the muscle fibers of the uterine wall, producing hemorrhagic areas over the surface of the uterus, the so-called "uteroplacental apoplexy" of Couvelaire. The toxemia, together with the hemorrhage which takes place, has a marked tendency to produce shock, or if shock is not actually present, it may develop quickly after any additional trauma. Such a patient is not a good surgical risk for cesarean section and especially Porro cesarean. Any additional trauma, such as manual dilatation of the cervix, a difficult internal version and extraction or a difficult forcep delivery, may precipitate a severe degree of shock which may be fatal. One of the deaths in this series occurred from shock within one hour after a forcep delivery complicated by a third degree laceration. The condition of this patient was apparently satisfactory before the delivery. If the case appears to be of the mild type and labor has begun, no interference is necessary, but the patient should be watched carefully for evidence of anemia or shock, and prompt treatment begun if indicated. Precautionary measures should include blood count, blood typing and matching for possible transfusion and preparation for intravenous or subcutaneous saline or glucose solution. Rupture of the membranes at the time the vaginal examination is made and the use of small doses of pituitrin will be indicated. If regular pains have not begun, it is certainly advisable to induce labor by the use of a bag.

If rapid delivery is contraindicated on account of the danger of shock and the case is of the severe type, what assurance is there that the patient will not die from hemorrhage during a slower process of delivery? Blood transfusion should be one of the most effective agents to combat the loss of blood and lessen the tendency to further hemorrhage. If a donor is not available, intravenous saline or glucose solution will be of considerable value. We may also rely to some extent on the fact that the bleeding from the open sinuses is checked considerably by the pressure of layers of clots underlying the placenta, and also by the fact that the intrauterine pressure is markedly increased by the tetanic condition of the uterine muscle. The presenting part tends to block the outlet and an increase in the intrauterine pres-



sure may be obtained with the abdominal binder, pituitrin or ergot. This is entirely different from the condition present in placenta previa, in which the bleeding from the open sinuses finds a ready exit and cannot be checked by pressure unless by the use of a large bag or by the body of the child after a Braxton-Hicks version.

It has been suggested that cesarean section is particularly indicated in cases of uteroplacental apoplexy, in which there is an extravasation of blood between the uterine muscle fibers, on account of the fact that a uterus so affected may not be capable of sufficient contractile power to control hemorrhage after delivery. There is no clinical sign or symptom which will enable us to diagnose this condition of the uterus without opening the abdomen. Furthermore, we know that in the great majority of cases the uterus does contract satisfactorily after delivery and can usually be safeguarded by massage, pituitrin, ergot, or packing.

A review of other statistics giving comparative results of radical and conservative treatment emphasizes the increased mortality associated with accouchement forcé and cesarean section. Appleton<sup>1</sup> advised against cesarean section on account of the patient being a poor surgical risk. He advocates conservative methods of delivery combined with supportive measures.

Frankl and Heiss<sup>2</sup> reported 34 cases, 16 of which were of the mild type and all patients recovered. Eighteen patients with severe symptoms were treated as follows: two patients by artificial rupture of the membranes; 4 patients by version and extraction; 4 patients by craniotomy and 7 patients by vaginal hysterotomy. There were nine deaths, a mortality of 50 per cent. The mortality in the series, as a whole, was 26.5 per cent.

Williams<sup>3</sup> reported 57 cases, of which 10 patients were treated by cesarean section. There were three deaths, all of which occurred in the group treated by cesarean section.

Fitzgibbons<sup>4</sup> reported 51 cases from the Rotunda Hospital. There were 8 deaths, a mortality of 15.7 per cent. The mortality was classified according to the treatment used, as follows: palliative, 10.7 per cent; packing, 12.5 per cent; cesarean section, 25 per cent; Porro cesarean, 66 per cent.

Brodhead<sup>5</sup> reported 34 cases of the severe type. There were 9 deaths, a mortality of 26.4 per cent. The mortality was classified according to the treatment, as follows: 8 cesarean sections with 3 deaths, a mortality of 37.5 per cent; 10 versions with 4 deaths, a mortality of 40 per cent.

Goethals<sup>6</sup> reported 128 cases with 11 deaths, a mortality of 8.6 per cent. Cesarean section was performed in 39 cases, with 6 deaths, a mortality of 15.3 per cent.

The average maternal mortality of the 65 cesarean section cases in the above reports is 22.6 per cent. Manual dilatation of the cervix; internal version and extraction, which may be difficult on account of the rigidity of the uterine muscle; a hard forceps delivery; craniotomy, which may likewise be very difficult, contribute greatly to shock and increased maternal mortality.

It is therefore best to induce labor in both mild and severe cases of

premature separation of the placenta, if pains are not already established, and allow labor to progress naturally throughout, meanwhile instituting such stimulative or supportive measures as may be indicated according to the patient's general condition. Rupture of the membranes and the use of pituitrin will usually bring about satisfactory progress. Breech extraction or low forcep delivery, if decided upon, should be performed with care to avoid all possible trauma. Manual removal of the placenta should not be resorted to unless the Credè method is unsuccessful and the hemorrhage excessive. This should seldom be necessary inasmuch as there is, rather, a tendency to spontaneous expulsion of the placenta. Intrauterine packing should not be used so long as the uterus manifests a reasonably fair state of contraction. For a period of some hours after the third stage, the patient requires the most watchful care, especially to maintain a well-contracted uterus, and to combat the earliest evidences of shock.

It is believed that the above management of premature separation of the placenta will offer the best prognosis, and furthermore, spare future pregnancies and labors the possible consequences of a weak uterine scar.

#### CONCLUSIONS

1. Premature separation of the normally implanted placenta is often accompanied by a degree of shock which is out of all proportion to the amount of hemorrhage.

2. Shock is more frequent in the cases accompanied by toxemia and is aggravated or precipitated by any trauma sustained during delivery.

3. The high fetal mortality accompanying premature separation of the placenta practically eliminates the fetus from consideration in the choice of treatment, unless delivery can be hastened without additional trauma and danger to the mother.

4. Induction of labor, watchful expectancy, stimulative and supportive treatment, offer the best prognosis. Shock, if present, should be treated first and labor then induced, if pains have not begun.

5. Cesarean section, manual dilatation of the cervix, internal version and extraction, or difficult forcep delivery are associated with an increased maternal mortality, especially in the severe cases.

6. The period of several hours following delivery is one of great danger for the patient and requires watchful care to combat shock or hemorrhage.

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# THE OCCURRENCE OF FUSIFORM BACILLI AND SPIROCHETES ASSOCIATED WITH A FOREIGN BODY IN THE VAGINA

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**I**N PREVIOUS communications I have shown<sup>1</sup> that in the smegma of normal women, fusiform bacilli and spirochetes were demonstrable in 58 per cent, but in the vaginal tract<sup>2</sup> these bacteria could not be found.

About the external genitals in certain erosive and ulcerative conditions, these organisms appeared in considerable numbers in the lesions. They often complicate the lesions of syphilis and chaneroids by causing more extensive necrosis. In ulcerating tumors they are often the cause of the necrosis and the putrid odor. In all of these lesions it was noted that these anaerobes were always associated with other bacteria particularly cocci, such as streptococci, and staphylococci, as well as colon bacilli, diphtheroids, and other organisms. Since these organisms were so often found in normal smegma, it appeared that normally they existed as saprophytes, but under certain conditions of the external genitals they could be pathogenic and give rise to ulcerating, necrotic and putrid lesions. In the normal vagina or in vaginal or cervical discharges, at no time could we demonstrate spirochetes and only in two instances were fusiform bacilli found.

In lesions of other organs we have particularly emphasized the importance of predisposing factors in the development of fusospirochetal infections. In the lung<sup>3</sup> it was observed that foreign bodies aspirated with mouth secretions lead to pulmonary abscess and gangrene of lung due to fusiform bacilli, spirochetes and associated pyogenic bacteria. Recently, foreign bodies were found in two patients with gangrene of the lung, in one a tooth lodged in the bronchus following a tonsillectomy, in another, a piece of concrete which had fallen into a bronchus of a mechanic while working under a truck. In both instances, large numbers of the anaerobes were demonstrated in the gangrenous abscess cavities.

In the following case, the fusospirochetal infection of the vaginal tract was associated with a foreign body that had been inserted by the patient.

Girl, nine years old, patient of Dr. Bartelt, entered the Lutheran Deaconess Hospital, because of very foul vaginal discharge, consisting of pus and blood, for a period of three months. Since her third year of age, it had been noted that the patient was decidedly subnormal mentally and on previous occasions had inserted foreign bodies into the ears and nose. It was therefore suspected that a foreign body might be present in the vagina as a definite history was obtained of repeated

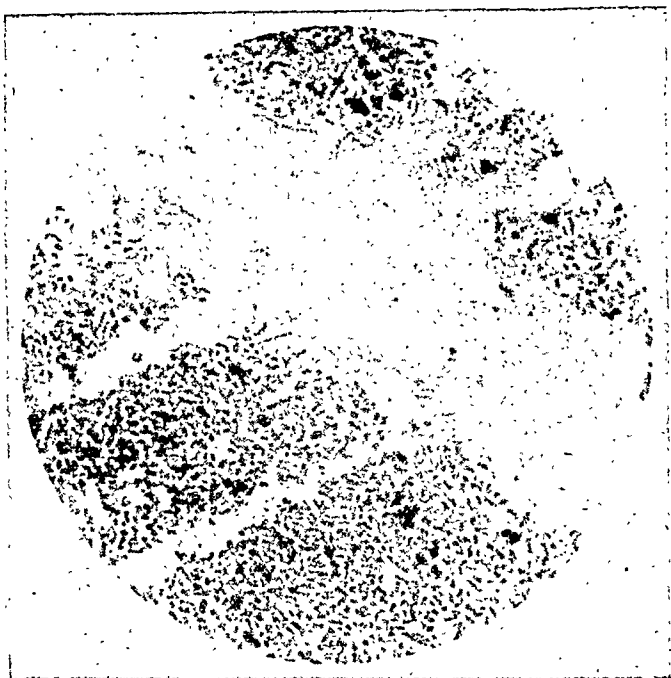


Fig. 1.—Many spirochetes and cocci; few fusiform bacilli.

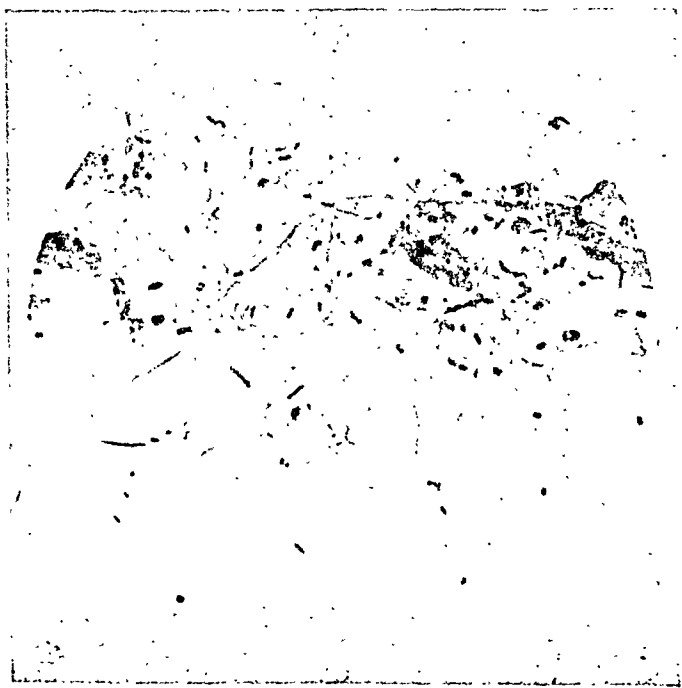


Fig. 2.—Fusiform bacilli together with a few spirochetes and diplococci.

finger insertion. Examination revealed intact hymen and an orifice admitting one finger, through which oozed a blood-tinged, very foul purulent discharge. A hairpin was felt in the interior, the blunt portion pointing backward toward the rectum, the free ends remaining free in the vagina. A smear and culture were made of the pus, carefully avoiding the external genitals. The hairpin was readily removed. Endoscopy was not attempted at this time. The patient did not return to the hospital but was seen at home ten days later. The discharge was markedly less and had no odor or blood. Subsequently, thirty days later, the discharge had completely disappeared.

Smears made of the discharge (Fig. 1), revealed many spirochetes, together with fusiform bacilli and many cocci and other bacilli. In aerobic cultures on blood agar, *Staphylococcus albus* and diphtheroids were identified.

The spirochetes were of varying lengths, some coarser, others finer, with 3 to 8 undulations. (Fig. 1.) From their morphology they could resemble the spirochetes from smegma or from the mouth. The fusiform bacilli (Fig. 2) were large, straight, long forms with pointed ends; a few were shorter and curved. Intermingled with the fusiform bacilli and spirochetes were numerous diplococci, short bacilli, and diphtheroids. (Figs. 1 and 2.)

The lesion was a chronic infection with fusiform bacilli, spirochetes; cocci, and other bacilli acting in symbiosis. While the cocci and other bacteria could very well produce the pus, the putridity of the discharge was due to the fusospirochetes. This has been our experience in other chronic types of infection in the lung, tonsils, middle ear, namely as in this case the fusospirochetes are always associated with pyogenic bacteria especially streptococci and staphylococci.

The occurrence of this fusospirochetal infection in association with a foreign body emphasized the importance of searching for underlying lesions and predisposing factors, either local or general, whenever the ulcerating area or the purulent secretions about the genitals contain the anaerobes in smear preparations.

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The authors report 18 cases of pregnancy complicated by carcinoma of the rectum and give complete follow-up histories including deliveries and the subsequent operations for the relief of the malignancies. In certain of the cases the carcinoma apparently developed simultaneously with the pregnancy and recurred later with subsequent pregnancies. Especially was this true in women with a definite carcinomatous tendency and family history, and in the presence of rectal polyps. The prognosis of such a complication of pregnancy is fair but could be improved if rectal examinations were carefully and immediately done upon all pregnant women who complained of rectal disturbances of any type.

RALPH A. REIS.

# REPORT OF A CASE OF PROLAPSED FIBROID WITH PARTIAL INVERSION OF THE UTERUS COMPLICATING THE PUERPERIUM

By W. F. GEMMILL, M.D., YORK, PA.

*(From the York Hospital)*

**I**NVERSION of the corpus uteri is of sufficient rarity to classify it as a medical curiosity. Graves states that it occurs once in 128,767 labors; Alice F. Maxwell states that 81.2 per cent resulted from uterine tumors; 2.2 per cent were idiopathic; 1.6 per cent followed abortions or premature labors. She has compiled statistics from 15 foreign clinics showing that the average number of uterine inversions is 1 in 123,364 labors.

The following case is of exceptional interest:

Mrs. H. L., multipara, aged thirty-two years, was admitted to the York Hospital, January 16, 1927, complaining of uterine bleeding. The following history was elicited.

Mild labor pains began Dec. 29, 1926, in the morning and continued until midnight, when the pains disappeared and were resumed again at 7:30 A.M. Delivery took place at 8:30 A.M., December 30, 1926, under light chloroform anesthesia.

The attending physician waited for uterine contraction and used the Credé method of expressing the placenta, but the patient had such a severe hemorrhage that the manual delivery of the placenta was deemed advisable.

On the third day following delivery, the patient passed some material which she thought was afterbirth and about one week later a large mass was seen at the introitus. The patient until this time had not complained of chills or fever.

A consultation was held and, as the patient refused to go to the hospital, the mass was reduced. On the third night, following the reduction of the mass, the patient suffered a severe hemorrhage and the husband gave her ergot; slight bleeding continued and a foul discharge developed. The temperature jumped to 106° F., and the pulse to 150. The patient was put in the Fowler position. Ergot and antistreptococcic vaccine were administered.

The mental condition remained clear and the pulse gradually approached normal, the temperature remaining, however, about 100° F.

The vaginal discharge became more and more offensive and there was very little lower abdominal pain but some meteorism.

On admission to the hospital, the pulse was markedly compressible and variable in quality and rate, ranging from 100 to 136 beats per minute. Blood pressure was 100 systolic, 55 diastolic, temperature 100° F. to 103° F. The urine was acid; sp. gr., 1,020; albumin, faint ring; sugar, negative; no red blood cells or casts but many pus cells. Blood examination showed 2,500,000 red blood cells; white cells, 7,400; hemoglobin, 44 per cent; polymorphonuclears 68 per cent; small mononuclears 24 per cent; large mononuclears 5 per cent. The Wassermann test was negative.

The patient presented a very anemic and toxic appearance. The skin was loose, although there was considerable adipose tissue and the abdominal muscles were quite flabby, due to her recent pregnancy. There was a moderate amount of tympanites.

On vaginal examination, a large mass the size of a fist protruded from the cervix. Evidence of gangrene was noticed, particularly on the posterior surface. The palpating finger could be swept around the cervical ring and demonstrated shortening of the left vertical diameter of the uterus.

Rectal examination revealed no cupping of the fundus uteri as one finds in total inversions of that organ; furthermore, the uterine body could be palpated on bimanual examination to be approximately normal in size and position.

Because of these findings, a diagnosis was made of prolapsed fibroid with partial inversion of the uterus, and an operation was advised.

Under ethylene anesthesia, a large boggy fibroid could be felt per vaginam, the size of a small grapefruit. The mass was sloughing and the posterior surface was quite gangrenous. Examination was made for the inverted uterine cornua and internal tubal ostia but without result.

The slight traction necessitated by this examination caused the pedicle of the fibroid to tear so that two clamps were applied, one on either side, and the pedicle above the clamps held with a suture ligature. The mass having separated from the pedicle by its own weight, the ligated stump was pushed above the cervical ring. Palpation of the left posterior region of the corpus revealed a large tear in the uterine wall and the ovary could readily be drawn into the rent. Direct inspection of the uterus through a midline incision revealed a large irregular opening extending from just below the left tubal ostium to the cervix. There was some blood in the culdesac. The left ovary was in close proximity to the torn area and was markedly edematous.

A supravaginal hysterectomy was done, clamp method, leaving in both tubes and ovaries, a drain was inserted extraperitoneally through the cervical stump and three cigarette drains placed in the culdesac protruded through the abdominal incision.

The pulse at the beginning of the operation was 120, at the end of operation 130, the highest point recorded was 150 during the forty minutes the operation was in progress. Digalen (m. xv) was given ten minutes after beginning the operation.

The patient had a stormy recovery and ran a septic temperature for six days. The abdominal wound partially broke down, and cultures revealed the *Staphylococcus aureus*. The patient was discharged in good condition on the thirty-fourth post-operative day.

The pathologic report is as follows:

Grossly the uterus shows the presence of a ragged tear 5 cm. in diameter, the wall is very much macerated, there is also a fibroid tumor 8 cm. in diameter. There is no evidence of malignancy, but the tissues are markedly gangrenous and show a pronounced inflammatory reaction.

135 EAST MARKET STREET.

## ENDOMETRIAL CYSTS OF THE OVARY

WITH THE REPORT OF A CASE CURED BY ASPIRATION AND  
X-RAY TREATMENT

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THE presence of endometrium-like tissue in the ovary, musculature of the uterus, rectovaginal septum, and in extragenital locations has been a source of more speculation than any other gynecologic condition in recent years. Many theories have been advanced to explain the origin of these heterotopic growths, but so far there is no one theory to explain all forms of endometriosis. There may be more than one etiologic factor concerned in their histogenesis.

Russell,<sup>1</sup> in 1899, was the first to report a case of endometriosis of the ovary. He held that the germinal epithelium is the source of these aberrant growths. Other investigators support this view on the ground that occasionally the cells of the germinal layer dip into the ovarian stroma and, when these ingrowths are cut off from the parent structure, they cannot be distinguished from endometrial glands.

Cullen,<sup>2</sup> in 1914, ascribed the origin of endometriosis to aberrant müllerian rests. Although these growths in the uterine wall can be traced to such origin, it is far-fetched to suppose that they are responsible for endometriomas that occur in extra-uterine parts of the pelvis.

Embryologic investigation shows that all genital epithelia are derived from the celomic epithelium of the urogenital fold. From it are derived the lining of the müllerian ducts, the germinal epithelium of the ovary, the follicular epithelium, and the pelvic peritoneum. The endometrium and endosalpinx must therefore be considered mere modifications of the pelvic peritoneum. Based on these facts, Lockyer,<sup>3</sup> in 1918, expounded the serosal theory. He believes that metaplasia of the peritoneal mesothelium is the etiologic factor in these aberrant growths, and that, being derived from the same mother layer, the pelvic peritoneum and germinal epithelium may, under perverted hormonal stimulation, show regional differentiation into endometrium or endosalpinx.

The serosal theory seems to be the most rational and can account for all forms of endometriosis, whether it be in the pelvic peritoneum, ovary, umbilicus, inguinal canal, rectovaginal septum, appendix, or abdominal scars following operations where the uterine cavity had not been incised.

Robert Meyer<sup>4</sup> is of the opinion that these growths are of inflammatory origin, pointing out that the serosa under such conditions is capable of forming gland-like structures because of its embryonal derivation. This theory is supported by M. T. Goldstein<sup>5</sup> and other observers.

Sampson,<sup>6</sup> in 1921, reported his first twenty-three cases of endometrium-like tissue in hemorrhagic ovarian cysts. He evolved the theory that these endometrial cysts owe their origin to implantation and subsequent growth of uterine epithelium which escaped together with menstrual blood from the fimbriated ends of the fallopian tubes. With the extensive employment of the Rubin test, the transplantation theory of Sampson received a serious set-back. One would expect an enormous



increase in the incidence of endometriosis in women subjected to transuterine insufflation. Though a few isolated cases of pelvic endometriosis following the Rubin test were reported, we have personally never observed a single case in nearly 1500 women whom we subjected to the Rubin test during the past seven years.

More recently Halban,<sup>7</sup> of Vienna, explained the existence of endometriosis on the basis of lymphatic distribution.

A discussion of the relative merits of the various theories concerning the origin of endometriosis is not within the scope of this paper. Passing mention of these theories was necessary in order to understand the rationale of the treatment instituted in the case herein reported.

Regardless of whether these growths are the result of lymphatic metastasis, peritoneal metaplasia, or seed implantation, there is no doubt of their endometrial nature. Their histologic structure, decidual reaction during pregnancy, and the characteristic cyclic changes they undergo during menstruation, make this view incontestable. The endocrine relationship that exists between the ovaries and the normal endometrium is evident in these growths. The continued activity on the part of ectopic endometrium in the presence of functioning ovaries, and the regressive changes it undergoes, when the ovaries are completely ablated, are matters of common knowledge. Thus Graves<sup>8</sup> reported four cases of obstructing rectovaginal adenomyomas cured by ablation of the ovaries. The diagnosis was established on microscopic evidence. Other investigators observed similar regressive changes in endometriomas involving areas of the rectum and bladder which could not be resected during the course of a panhysterectomy. These facts indicate that the activity of misplaced endometrial tissue ceases when deprived of the activating influence of ovarian hormone. Although ablation of the ovaries and irradiation were successfully used in the treatment of solid endometrial tumors, a perusal of the literature does not disclose a single case in which aspiration of the contents of endometrial cysts with subsequent irradiation was ever employed in the treatment of this condition. The following case is of sufficient interest to warrant recording.

S. S., aged forty-five, a mother of four children, was admitted to the Mount Sinai Hospital on August 31, 1927, complaining of pain and distention of the abdomen, more marked with the advent of the menstrual flow. Her family and past history are irrelevant. The patient weighed 214 pounds. She had many decayed and abscessed teeth, hypertrophied and infected tonsils, and chronic pansinusitis. The pulse was 120, blood pressure comparatively low, cardiac muscle tone poor. A large intraperitoneal cystic mass reaching three fingers above the umbilicus, and some edema of the abdominal wall and lower extremities were noted. Vaginal examination showed the uterus only slightly enlarged and pushed to the left by the mass described above. There was a moderate secondary anemia. Blood chemistry and Wassermann test were negative.

After preoperative rest in bed and the administration of digitalis, the patient was prepared for operation under spinal anesthesia. Because of a few unsuccessful attempts to introduce the anesthetic, her pulse became too rapid and feeble to warrant an attempt at operation under a general anesthetic. In order to relieve

the embarrassed myocardium, aspiration of the cyst as a temporary measure was deemed advisable. This yielded five quarts of tarry chocolate-colored fluid. It dawned on us that we were probably dealing with an endometrial cyst. We therefore resorted to intensive x-ray treatment in the hope of causing regressive changes in the cyst wall by withdrawing the hormonal influence of the remaining ovary and through the direct action of the rays on the cyst wall.

The patient made an uneventful recovery and on discharge from the hospital, four weeks later, only a small, not tender mass was palpable to the right of the uterus. This mass gradually disappeared under the influence of repeated x-ray treatment so that there is, at present, no evidence of adnexal pathology.

We realize that the mere recovery of thick chocolate-colored material from an ovarian cyst does not justify the diagnosis of endometriosis and that it is rather hazardous to subject an enormous sac of a simple hemorrhagic cyst to intensive irradiation. Microscopic examination of the aspirated fluid rarely gives a clue as to the structure of the cyst wall. The shrinkage and final disappearance of the sac when the hormonal influence of the remaining ovary was withdrawn under the influence of irradiation is positive proof of its endometrial nature. The general condition of this patient was such that no measure at our disposal could equal the risk of an abdominal operation.

Our past experience with huge hemorrhagic cysts of the ovary led us to believe that the cyst wall, in this case, was most probably of endometrial origin. On two previous occasions we encountered chocolate-colored fluid when needling the abdomen to differentiate between general peritonitis and encysted fluid. In one case the endometrial cyst was twisted on its pedicle, giving rise to board-like rigidity of the abdominal wall usually seen in general peritonitis. The appearance of the aspirated fluid justified immediate operative interference. In the other case, the cyst contents had undergone infection which gave rise to symptoms of diffuse peritonitis. Subsequent examination of the cyst wall in both cases corroborated the diagnosis of endometriosis. The history of cyclic abdominal pain coincident with menstruation was another factor in leading us to suspect the endometrial nature of the ovarian cysts recorded.

This method of treating large endometrial cysts of the ovary is applicable in women near the menopause and in those upon whom an abdominal operation is too hazardous to undertake because of some serious constitutional condition.

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## SIMPLE ROUND ULCERS OF THE VAGINA

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THE term "ulcus rotundum simplex vaginae" was first used by Zahn in 1884 to describe an ulcerative lesion of the vaginal wall which he noted as an accidental finding during an autopsy. The condition has since been observed a few times on living patients, but it is unusual in occurrence and seems to have attracted but little attention. A search of the literature fails to reveal any case reported in this country, and the only detailed account that has been published since 1904 is that of Schroeder and Kuhlmann, which appeared in 1922. The object of the present study is to give a review of the subject and to report two additional cases.

### HISTORICAL

Five of the 16 cases of simple round ulcer of the vagina which have been reported were observations made as accidental findings at autopsy. The first instance was described by Zahn<sup>1</sup> in 1884. The patient was a woman of seventy-six years, who died following a right-sided contracture of the extremities and aphasia. She had been in the hospital six years and no indication of a pelvic abnormality had ever been found. At autopsy an ulceration was discovered in the upper part of the vagina on the posterior wall and somewhat to the left of the midline. It was superficial, almost circular in shape, measured 2.5 by 2.3 cm., was sharply demarcated, and the base was hyperemic and covered with a thin layer of purulent material. There was no induration about the ulcer. Microscopically, nothing remarkable was seen besides connective tissue markedly infiltrated with round cells. The uterine and vaginal arteries were sclerotic and the size of the lumina was much diminished, while an arterial branch leading to the region of the ulcer was completely obliterated.

Browicz<sup>2</sup> in 1888 described the findings in the vagina of a woman of fifty-nine years who had died of croupous pneumonia. In the right posterior part of the portio vaginalis he found a smooth circular area, sharply limited, of a grayish to a brownish black color, which represented a superficial ulceration. There were, in all, eight similar small spots in various parts of the vagina. Microscopic examination showed necrotic tissue, and a study of the blood vessels in the neighborhood showed an obliteration of their lumina.

Zahn<sup>3</sup> published a description of a second case in 1889. The patient, aged fifty-one, had died of endocarditis and chronic pulmonary tuberculosis. The findings in the vagina were "chronic atrophic vaginitis with ecchymosis and hemorrhagic erosions; ulcus rotundum simplex incipiens." This ulcer, again, was found posteriorly to the left of the midline and just below the external os, and measured 2.0 by 1.0 cm. It is described as a brownish area, somewhat depressed from the surrounding mucosa and with sharp edges. The author considered this finding as an incipient ulcer and mentions other similar fine spots, brownish in color and with a central depression, on the right and anterior walls of the vagina. There were, in addition, marked endarteritic changes in the uterine and vaginal arteries.

The first published observation of this type of ulceration in the living woman seems to have been made by Braithwaite<sup>4</sup> in 1894, although he was unaware of the preceding work of Zahn and Browicz. In a paper entitled "Destructive Ulceration of the Vagina," he described two types of vaginal ulcers which he had seen, and subsequent writers (Beuttner, Veit, Schroeder and Kuhlmann) have accepted one of these as belonging to the category of simple round ulcer. He mentions two cases. The first was a woman fifty-five years old, who had been living under bad hygienic conditions, and had some time before had an enucleation of an eye for a low grade infection. On pelvic examination he noted four or five narrow ulcers on the posterior wall of the vagina, which coalesced and gradually spread until the whole lower half of the vagina was involved. There was no slough over the ulceration, the edges were sharp, and there was no induration. The patient recovered following topical applications, general hygienic care, and a restful vacation in the country. The author then states that he saw a second case, but he does not give any details beyond the statement that there was an ulceration of the posterior vaginal wall of the same nature as described above, although not quite so extensive. The patient soon left the hospital unimproved and was lost sight of.

In 1895, von Skowronski<sup>5</sup> described the third case observed on a living woman. The patient, aged thirty-seven, complained of pain in the region of the urethra, and frequency and burning on micturition. Pelvic examination showed a shallow, round ulcer the size of a "half-kreuzer" on the anterior vaginal wall 1.5 cm. from the urethra, which was sharply defined, and covered with irregular necrotic granulations. The ulcer was excised, and the microscopic examination revealed a sharp breaking off of the mucosa at the edge of the ulcer; the base was made up of necrotic tissue; the submucosa was still recognizable here and there; the blood vessels showed a typical picture of obliteration of the lumina.

In 1896, two additional cases found at autopsy were reported from Zahn's laboratory by Beuttner.<sup>6</sup> The first instance was a woman of forty-four years, who had died from cardiac disease. An ulcer measuring 1.5 by 1.2 cm. was found on the posterior vaginal wall somewhat to the left of the mid-line and 3 cm. below the cervix uteri. The edges of the ulcer were sharply defined and were undermined only at one extremity. There were numerous ecchymotic erosions of the vaginal wall. The second case was a woman of fifty-eight years who also had died of heart disease, and at autopsy, among other anomalies, was found an ulcer of the duodenum, ecchymotic erosions of the large intestine, a small uterine fibroid, and a mucous polyp of the cervix uteri. In about the same situation in the vagina as in the previous case he found a triangular scar, slightly elevated from the surrounding mucosa, and measuring 7 by 5 by 6 mm. From this region a narrow band of scar tissue 6 mm. broad led upward to the external os.

Bekmann<sup>7</sup> reported a case in 1897 occurring in a woman sixty-four years of age, who complained of leucorrhea. The ulcer was slightly larger than a "6 sous," round but not quite regular, very shallow, sharp edges, with reddish base covered with yellowish detritus, and was situated in the posterior culdesac slightly to the right of the midline. The ulcer was excised, but the wound broke down and healing only took place by secondary intention. The histologic study showed a sharp breaking off of the mucosa, the surface of the ulcer looked like granulation tissue with extravasation of blood and areas of necrosis, and a marked infiltration with small round cells. An endarteritis was present in the blood vessels, but no definite obliteration of the lumina could be demonstrated. In one area there were dilated capillaries.

Two cases were described by Thomson<sup>8</sup> in 1904. The first was a young woman aged twenty-two, with pain in the lower abdomen and dyspareunia. The ulcer was 1 cm. in diameter, and was found on the posterior vaginal vault somewhat to the left. It was sharply defined, the base was reddened, and no induration was de-

monstrable. The patient had a marked accompanying anemia. The ulcer was treated with the thermocautery, but it did not show much tendency to heal after this and the author then lost trace of the patient. A small piece had been removed from the wall of the ulcer, which microscopically showed a vascular connective tissue with slight round cell infiltration. In some places the epithelium was thickened. The second patient was a woman aged thirty-one who complained of profuse menstrual periods and pain in the lower abdomen. She was not well nourished, and was somewhat anemic. On the posterior vaginal wall was a shallow ulcer with sharp edges, which in size admitted the finger tip. The lesion healed spontaneously.

In their paper, Schroeder and Kuhlmann refer to a case reported by Puech<sup>9</sup> in 1905. Although this reference is given in one or two journals of the time, it cannot be found in the *Index Medicus*, and the journal in which it appeared seems to have been unknown in this country. No description of this case, therefore, is available for this review.

In the edition of his textbook published in 1908, Veit<sup>10</sup> refers to this condition and mentions having seen two cases in living women. He does not give any details except that the histologic examination in one patient showed an associated senile vaginitis.

Schroeder and Kuhlmann<sup>11</sup> gave a very complete account of one case in 1922. The patient was forty-one years old and applied for treatment because of a "bearing down sensation" and leucorrhea. The ulcer was found just behind the frenulum labiorum posterius. It was almost circular, 2 mm. in depth and 1 cm. in diameter. The edges were sharply defined, not undermined, and the base had a "yellowish, glassy, fatty" appearance. The surrounding mucosa was essentially normal. There was very slight induration around the ulcer. The treatment consisted of excision. The histologic picture showed the base to be covered with fibrin, and under this surface was a granulation tissue infiltrated with polymorphonuclear leucocytes. The vessels were thin-walled, without hyaline changes or perivascular thickening, and were surrounded by round cells and polymorphonuclear leucocytes. There were inflammatory cells deep in the musculature. The epithelium extended to the edge of the ulcer without any undue thickening, and shortly before it reached the ulcer itself, it gradually thinned out. Plasma cells were demonstrable. Deep tissue necroses, epithelioid cells, giant-cell formation, hyaline degeneration of the vessels, could not be found at any point. No tubercle bacilli, *Spirocheta pallida* or Ducrey's bacilli were demonstrable by specific stains.

In his textbook on *Special Pathology*, Kaufmann<sup>12</sup> refers to the paper by Schroeder and Kuhlmann and states that reddish demarcated areas of necrosis may be found at an early stage of this disease and that he saw several in the vagina of one woman eighty-seven years of age.

#### CASE REPORTS

The following case has recently come under the observation of the Stanford Gynecologic Service at the San Francisco Hospital:

CASE 1.—Mrs. L. B., aged forty-nine, gravida iii, para iii; menopause two years ago. Admitted March 5, 1929, complaining of profuse vaginal bleeding of two days' duration.

General physical examination showed no abnormalities relative to present complaint, except a marked secondary anemia. Blood count gave R.B.C. 1,420,000, W.B.C. 7,400, and hemoglobin 50 per cent. No abnormal cells seen in differential count. Wassermann reaction negative.

On pelvic examination there were no pathologic findings associated with the uterus and appendages. Speculum examination showed a superficial ulceration,

oval in shape, 3 cm. long by 1.5 cm. wide, situated on the left vaginal wall about midway between the vault of the vagina and the outlet. The edges were sharply demarcated, there was no undermining, and the base was covered with a fibrinous exudate. The surrounding mucosa was pale, and there were a number of punctate hemorrhagic spots in the vault of the vagina.

The patient was bleeding profusely from the ulcer, a tight vaginal pack was used to control the hemorrhage, and she was given a blood transfusion.

On March 19, a portion of the ulcer was excised for microscopic examination. The patient's general condition gradually improved, and on March 27 the blood count showed 2,200,000 red blood cells, although the hemoglobin was only 35 per cent. Since her admission she had also run a febrile course, the afternoon temperature varying between 99° and 100.5° F.



Fig. 1.—Simple round ulcer of the vagina. First case.  $\times 100$ .

Following a pelvic examination on April 1, profuse bleeding again set in and could only be controlled by a series of vaginal packs. The patient was given another blood transfusion, and topical applications of a weak solution of silver nitrate were used in the vagina. Her condition now rapidly improved, and examination on April 19 showed the ulcer to be healing rapidly, although other hemorrhagic erosions of the vaginal wall were seen. On April 29 healing had progressed to such a point that it was felt she could be discharged from the hospital. On May 9 the ulcer was completely healed, and subsequent examinations failed to show any tendency to recur.

The histologic examination of the biopsy specimen from the ulcer showed chronic inflammatory changes (Fig. 1). The vaginal mucosa was essentially normal, except for a subepithelial infiltration with round cells in the neighborhood of the ulcer, and the epithelium gradually thinned out as it approached the edge of the lesion. The base was composed of a thin layer of connective tissue resting on muscle and

fat. There was a slight infiltration of the whole area with polymorphonuclear leucocytes, lymphocytes, and sections stained with methyl-green pyronin showed the presence of a considerable number of mast-cells. In one area near the surface there were numerous small blood vessels, and deep-seated arteries showed endarteritis. There were no deep necroses, tubercle formations, tubercle bacilli, etc., demonstrable by special stains.

A search through the records of the Stanford University Gynecologic Service shows that a similar case was seen in the Lane Hospital in 1916. The history is complete, and the sections are still available for examination.

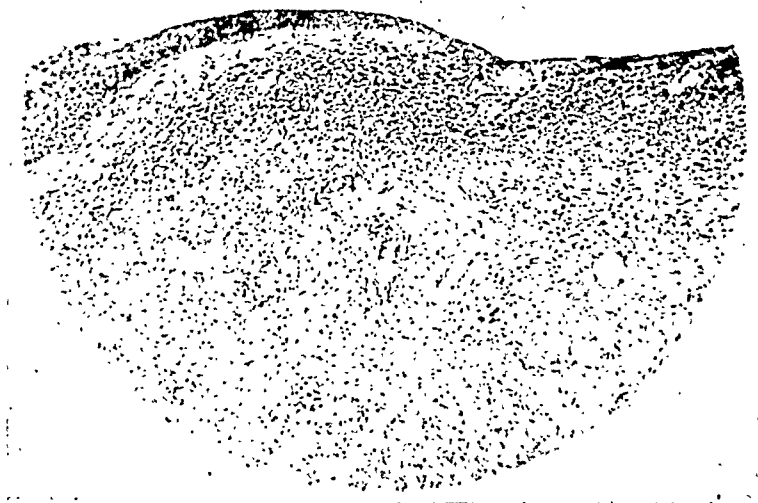


Fig. 2.—Simple round ulcer of the vagina. Second case.  $\times 100$ .

CASE 2.—Mrs. K. L., aged sixty-three, gravida ii, para ii, menopause twenty-three years ago. Patient had been under the care of the Neuropsychiatry Department for numerous complaints, and was referred to the Gynecologic Department because of burning and frequency of micturition. Cystoscopic examination pointed to a possible left-sided pyelitis, and the culture of the urine gave *B. coli communis*. Wassermann reaction was negative. Blood count normal.

Pelvic examination showed no abnormalities of the external genitalia; the uterus was small and atrophic, and nothing unusual was noted in the appendages. The vagina was small and seemed normal to palpitation, but on speculum examination a superficial ulcer was seen in the left fornix. It was slightly irregular in shape, measured 1.0 by 0.8 cm., the edges were sharply demarcated but not undermined, there was no surrounding induration, and the base was clean, granular, and of a pinkish color. Another similar ulcer of approximately the same size was seen in the right fornix. The surrounding vaginal mucosa appeared normal for a patient of her age.

A biopsy specimen was obtained from the ulcer on the right side, and the lesions were then treated by topical applications of a solution of silver nitrate. They healed rapidly and were no longer visible a few weeks after they had first been noted.

The histopathologic examination showed an atrophy of the vaginal mucosa, which thinned out gradually as it approached the edge of the ulcer (Fig. 2). The base was composed of connective tissue, and there was a much more extensive infiltration with polymorphonuclear leucocytes and lymphocytes than in the previous instance. There were also numerous eosinophiles and a number of plasma cells. The blood vessels showed no remarkable features, but an increase in their number was noted in the region of the ulcer. As in the first case, there were no extensive necroses, no tubercle formations, and special stains for tubercle bacilli were negative.

#### SUMMARY AND DISCUSSION

The *ulcus rotundum simplex vaginae* is to be regarded as a rare lesion. It has been observed only once in 4666 hospital admissions on the gynecologic service of Lane Hospital. The age incidence is known in 14 of the 18 reported cases, and all but 3 of the patients were over forty years of age, while 4 of these were over sixty. There is apparently no connection between this lesion and other pelvic disease, the only exception being Beuttner's second case, where a small uterine fibroid and a cervical polyp were found. In several instances, however, general systemic conditions were described. Zahn's first case died with a contracture of the extremities and aphasia, for which she had been in hospital six years; both Beuttner's patients had cardiac disease, and autopsy in one case showed in addition an ulcer of the duodenum and ecchymotic erosions of the large intestine; Browicz' case had a croupous pneumonia; Zahn's second, an endocarditis and chronic pulmonary tuberculosis; one of Braithwaite's, a general asthenia; and Thomson's first case and one of mine, a marked secondary anemia.

The ulcer is a chronic lesion, and in most cases there were few or no associated symptoms. It may produce a leucorrhea, there may be some bleeding, and although it is generally painless this is dependent on the site of the ulcer, but any manipulation may elicit tenderness. It is characteristically round or oval in shape; its edges are even, sharply demarcated, and there is no undermining; it is very shallow in depth; there is no surrounding induration, and on palpation it may be missed altogether. The base is usually smooth, reddened, and has the appearance of granulation tissue, or it may be covered by a fibrinous or purulent exudate. The surrounding vaginal mucosa appears normal, although in Zahn's second patient there was an extensive ecchymosis and hemorrhagic erosion, in one of Veit's there was a senile vaginitis, and in my first case there were fine punctate hemorrhagic spots in the vault of the vagina. Of thirteen instances in which the site of the ulcer is known, it occurred eleven times on the posterior vaginal wall, and once on each of the anterior and lateral walls. It was just to the left of the midline on the posterior wall in 6 cases, and Beuttner ex-



plains this feature as being the site where the secretions from the cervical canal are poured out. The lesion is invariably single, although in one of my cases there were two ulcers, in Browicz' there were eight, in Braithwaite's there were four or five which gradually coalesced, and Kaufmann noted a large number of areas of necrosis in his patient.

A detailed histopathologic study of this lesion has apparently only been made in 9 cases, and showed no special features which would establish its identity from any superficial chronic inflammatory ulcer. The surrounding mucosa presents no marked changes, and either breaks off suddenly at the edge of the ulcer or thins out gradually. The base is composed of granulation tissue, it may be covered with fibrin or purulent material, and there is a moderate infiltration with polymorphonuclear leucocytes, lymphocytes, and sometimes plasma cells and mast-cells. The ulcer is shallow and there is no extensive necrosis of the underlying muscle and fatty tissues. In 5 cases a thickening of the walls of the surrounding vessels with obliteration of the lumen was described.

A number of theories have been advanced to account for the etiology of the simple round ulcer of the vagina. Zahn and most of the earlier authors were much impressed with the endarteritic changes in the blood vessels accompanying these lesions and were convinced that they were the most important factor. It must be remembered in this connection, however, that most of these patients were at an age when such vascular changes are frequent, and on the other hand the occurrence of these ulcers is very unusual. A bacterial origin, and the possibility of trauma during coitus or following the introduction of a foreign body, have also been suggested. Schroeder and Kuhlmann advance the theoretical consideration of a pathologic change in the vaginal secretion as a possible factor. As these authors assert, however, it must be remembered that the *ulcus rotundum simplex vaginae* is not a specific type of lesion but simply a chronic inflammatory ulcer which has assumed a particular form in the vagina.

The differential diagnosis is of importance and is given in detail in Schroeder and Kuhlmann's monograph. They distinguish nine types of ulcers besides the one described in this paper. (1) The *phagedenic* ulcer, a variety allied to the simple round ulcer and first mentioned by Clarke<sup>13</sup> in 1821 as a "corroding ulcer of the os uteri." It is recognized by its irregular form, its thickened hard edges, extensive tissue destruction of the cervix and vagina, and profuse accompanying hemorrhages. A similar type has also been described as the *aphthous* ulcer. (2) *Tuberculous* ulcer. (3) *Syphilitic* ulcer. (4) *Chancroid* ulcer. (5) *Dysenteric* ulcer. (6) *Diphtheritic* ulcer. (7) *Uremic* ulcer. (8) *Chemical* ulcer. (9) *Varicose* ulcer. To these may be added (10) *traumatic* ulcer, to include those forms seen following the injudicious use of pessaries, postoperative ulcerations, etc.

Owing to the few observations of this disease there is no general agreement as to the most satisfactory method of treatment. Total excision was done in 3 cases with healing by primary intention on one occasion. Treatment with the cautery was attempted once, but with no success. Four cases are known to have done well by simple local applications and general hygienic care of the patients. In both instances reported in this paper the lesions healed readily with topical applications of a weak solution of silver nitrate, but one patient remained in bed in hospital for several weeks. It would seem that a conservative method of treatment with excision as a last recourse would be the most logical procedure.

#### CONCLUSIONS

A review of the literature shows that 16 cases of *ulcus rotundum simplex vaginae* have previously been mentioned. Two additional instances are reported.

The lesion is a chronic nonspecific inflammatory ulcer of the vagina, which usually occurs after the age of forty. The etiology is not understood.

The differential diagnosis consists in recognizing it from ten other ulcerative conditions which may occur in this situation.

Treatment by conservative means is recommended.

My thanks are due to Mr. Pierre Lassègues for the technical work connected with this study.

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STANFORD UNIVERSITY HOSPITAL.

## THE INCIDENCE OF UNDULANT FEVER IN PREGNANCY AND ABORTION

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THE senior author became interested in the subject of undulant fever, first, because of an attack of the disease, and second, through the writings of Hardy. It was thought possible that undulant fever might be overlooked in pregnant patients, especially in those who abort. The Research Division of the Chicago Department of Health was consulted and a plan outlined to determine if the blood of pregnant women in this locality would react to *Brucella abortus* or *Brucella melitensis* antigens.

The blood specimens taken for the Wassermann test from patients applying to the prenatal clinics of the Chicago Lying-In Hospital and Dispensary and the Cook County Hospital were used. All patients in the series who aborted during this time were also included. Most of them were women who had had a criminal abortion performed. The patients were from the middle and lower classes of the Chicago district, including whites, colored people, and Mexicans. They lived in all sections of the city and, therefore, present a rough cross-section of the population.

In 1928, 6 cases of proved undulant fever were reported in Chicago. None of these had been in direct contact with farm animals, so far as could be learned, and all were city dwellers. Since the market milk supply of Chicago consists only of pasteurized milk (99 per cent) and certified milk (1 per cent), the possibility of milk-borne infection seems unlikely and the question of how the infection was contracted remains open.

The literature on the subject of the source of human infection is somewhat at variance. On the one hand, definite contact of human cases of undulant fever with infected cattle and with the raw milk of infected cattle, has given rise to the belief that human infections are often of bovine origin. On the other hand, it is pointed out that other groups of persons in constant contact with the bovine disease and drinking the raw milk of such animals for many years have not developed the disease. Laboratory data, though as yet meager, seem to indicate that the organism commonly found in human undulant fever corresponds more closely to the porcine type of *Brucella* than to the bovine. Further data based on detailed type studies of the *Brucella* encountered are needed to solve this problem.

Clinically the senior author knows of 28 cases of undulant fever among college students which were thought to be contracted by drinking raw milk from a herd found to be badly infected with *Brucella abortus*. It is not known whether the organism conformed culturally to the bovine or porcine type. Epidemiologic evidence, however, pointed to infected raw milk as the apparent agent of transmission in these 28 cases.

In Chicago the etiology of the disease is not clear, since all market milk except certified is pasteurized and it is generally conceded that pasteurization is an effective protection. The senior author suggests the following sources of infection as possible factors in the dissemination of the disease.

(A) *Liver and Meat*.—Liver is eaten by a great many people because of the present fad. The supply of calves' liver does not equal the demand, so beef liver and pigs' liver are being offered by the meat packers. Such products are not always thoroughly cooked, especially when put up in the form of sausage and similar edibles consumed without further heating. We know that pigs and cows suffer from the disease and that the infecting organism is present in the blood. Hence it is conceivable that the disease may gain access to the human body through uncooked or partially cooked meat and liver from infected cows and pigs.

(B) *Certified Milk*.—In spite of all the precautions taken by certified milk producers, this product cannot at present be eliminated as a possible source of contagion. Conclusive data, sufficient to establish its rôle, are not as yet available.

In 1917 De Forest<sup>1</sup> wrote on "Infectious Abortion in Cattle, as a Complication of Pregnancy in Women." In the cases reported by him the connection between *Brucella abortus* in cattle and the abortions in women is based on clinical and epidemiologic evidence only. Theoretically it seems possible that some abortions in women may be due to undulant fever.

Perhaps those patients who do not make a good recovery following an abortion may owe their long illness to this cause. The increasing number of undulant fever cases in this country should soon afford means of solving the question.

We are making a study of all abortion cases both spontaneous and criminal coming under our observation. Cultures are being made from the aborted material and agglutination tests are being run.

*Experimental Work*.—One thousand and fifteen blood specimens from pregnant women were tested by the macroscopic agglutination method with polyvalent *Brucella abortus* and *Brucella melitensis* antigens. The serum was separated, inactivated and submitted to the Health Department laboratories for test. The macroscopic agglutination test used was essentially that described by A. V. Hardy<sup>2</sup> of Iowa

City, Iowa, with the modification that the suspensions were formalinized for preservation and safety in handling. This was done by adding one-half of one per cent of neutral formalin solution as suggested by I. F. Huddleson.<sup>3</sup>

Previous to adoption of the formalinized antigen for routine purposes, nine known positive and a number of known negative sera were run in duplicate in cooperation with Mr. Hardy, using formalinized antigens prepared by us and nonformalinized antigens prepared by him. The formalinized antigens were eight months old and the nonformalinized antigens two weeks old at the time of the check test. All agglutination results, both positive and negative, were identical in this series for each type of antigen.

The cultures used for the antigens were as follows:

*Brucella abortus* 705, isolated in England and designated by Huddleson as *Brucella abortus* 172.

*Brucella abortus* 456, isolated from a cow's fetus and supplied by the Bureau of Animal Industry, U. S. Department of Agriculture, Washington, D. C.<sup>4</sup>

*Brucella melitensis* 803, isolated from a guinea pig, inoculated with goat's milk and supplied by the Bureau of Animal Industry, U. S. Department of Agriculture, Washington, D. C.

*Brucella melitensis* 428, supplied by the Pasteur Institute of Algeria; source of isolation apparently unknown.<sup>4</sup>

To prepare the antigens, cultures were planted in beef liver infusion agar (Stafseth and Huddleson<sup>5</sup>) in large test tubes, by seeding with a loopful of organisms from a stock culture. The tubes were incubated for forty-eight hours at 37° C. The growth was suspended in sterile distilled water containing 0.5 per cent of neutral formalin. Approximately 15 c.c. of the formalin solution were added by means of a sterile pipette to each tube of culture, and after this treatment smears were made to check the purity of the organism. Extreme precautions should be taken in these procedures to avoid exposure to infection and contamination of the material. Each tube was mixed by rolling in the palms of the hands and the suspensions transferred to large sterile flasks. The flasks were shaken from time to time for two days and then placed in the ice box for five days. Tests for sterility were made on the seventh day, and if found sterile the antigen was filtered and standardized by matching to turbidity No. 4 of Kober's nephelometer.

The agglutination tests of the series were carried out in  $\frac{1}{4}$  by 6 inch tubes. Known dilutions of inactivated sera of 1 to 5, 1 to 20, and 1 to 50 were prepared in saline solution and one-half c.c. amounts placed in the test tubes. One-half of one c.c. of standardized antigen was then added to each tube. The tubes were shaken vigorously for about thirty seconds, placed in a water-bath at 37° C. for four hours and then put on ice overnight. Readings were made on the following morning and recorded as described by Evans.<sup>6</sup>

Results: Of the 1,015 blood sera from pregnant women subjected to agglutination test with the antigens of *Brucella abortus* and *Brucella melitensis*, none gave definitely positive results and only five gave slightly positive reactions. The reactions of these five are given in Table I.

Clinically, there was no premature interruption of pregnancy in any of these 5 patients, and they were apparently enjoying the best of health. They had never had any illness that suggested undulant fever. Two have since been delivered at full term, both having normal children. The detailed history of these patients is not given because none shows anything of interest bearing on the subject.

TABLE I

LABORATORY NUMBER	DILUTION		
	1/10	1/40	1/100
28	++++	++++	0
132	++++	0	0
468	++++	0	0
724	++++	0	0
847	++++	+++	0

Twenty-three cases of abortion in women were studied. Of these, the sera of 22 patients were negative to the agglutination test. One gave a weakly positive reaction with placental blood. In 6 cases in which the placental material was submitted, cultures were also made. The cultural methods used were those described by Evans<sup>c</sup> except that a duplicate was run in a tube sealed with paraffin to retain carbon dioxide, to permit growth of the bovine type of *Brucella*. None of the cultures yielded *Brucella abortus* or *Brucella melitensis*.

The one patient whose placental blood agglutinated the antigens in low dilutions, gave a history as follows:

Mrs. K., aged thirty-five, married two years; had measles, whooping cough, followed by mumps, otitis media, ten years ago; influenza in 1918. No typhoid. Surgically negative. Patient went to Europe June 1, 1928, for five months. While in Paris she noticed the onset of malaise and that she perspired very easily. She had no temperature or chills at this time. These symptoms continued until her arrival in the United States November 1, 1928. Since that time the patient noticed that she became tired very easily and was drowsy a good deal of the time. October 18, during voyage, patient had her menstrual flow for one day. Three days later she had severe cramps and passed many clots. This continued for twelve days. Her last period occurred November 20, 1928. She aborted January 27, 1929, after suffering from bleeding and cramps for one week. Curettage yielded only a small amount of tissue, which was sent to the laboratory for examination. The culture for *Brucella abortus* was negative. The agglutination test with vaginal blood gave a positive reaction in a dilution of 1-80. A venous blood test taken one week later was reported negative by two laboratories.

In the Chicago Health Department laboratories, agglutination tests for undulant fever have been run routinely for some time past on all blood specimens submitted for the Widal test. Six hundred and fourteen such tests have accumulated (418 microscopic and 196 macroscopic tests). Of these, 608 were negative and 6 positive.

All the 6 cases represented persons in which a clinical diagnosis of undulant fever was made or suspected by the patients' physicians. Sera

from these 6 patients agglutinated the formalinized antigens in dilutions of from 1 in 300 to 1 in 2,000. The histories of three of the cases indicated infection originating out of the city. In two others we were unable to establish definite animal contact other than the indirect contact of using foreign cheese or certified milk as food. Unfortunately, cultures were not obtainable from these patients for study of the type of organism.

#### SUMMARY

1. One thousand fifteen blood sera from pregnant women were tested by the agglutination reaction with *Brucella abortus* and *Brucella melitensis* antigens.

Of this number none gave definitely positive and only 5 weakly positive reactions. The indicated conclusion is that *Brucella abortus* infection is not generally prevalent in pregnant women in Chicago.

2. Blood sera from 22 women who had aborted gave negative results by the agglutination test with *Brucella abortus* and *Brucella melitensis* antigens. In the twenty-third case the aborted blood gave a positive reaction in a dilution of 1-80, while the venous blood test was negative. Cultures from the placental material also gave negative results.

In a later paper we will give a more complete report on the relation of the Genus *Brucella* to human abortion in Chicago.

3. Of the six clinical cases of undulant fever confirmed in the Health Department Laboratory, only one patient was a female. This patient had given birth to a normal child at full term three months before becoming ill and gave no history of a previous abortion.

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122 SOUTH MICHIGAN AVENUE.

## PREGNANCY COMPLICATED BY AMYOTROPHIC LATERAL SCLEROSIS\*

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*(From the Clinic of the Woman's Hospital)*

I AM reporting this case because, in a search of the literature of the past twelve years, I have been unable to find any references to the occurrence of pregnancy in patients with this disease.

Amyotrophic lateral sclerosis is not uncommon, as evidenced by the constant presence of several cases on the Neurologic Service at Bellevue Hospital. It usually affects those in the middle part of adult life; it does, however, according to standard textbooks, occasionally occur during the childbearing period. From this fact the following question seems pertinent: If it does take place during the childbearing period and the patient becomes pregnant, should the pregnancy be terminated? And further, if it should not be interrupted, what is the outcome of the pregnancy as regards the condition of the mother and baby?

Inasmuch as this patient was unable to talk distinctly, the following history was obtained from the husband. Mrs. E. C., aged thirty-nine years, believing she was in active labor, was admitted to the Woman's Hospital February 16, 1926. She came from healthy parents and her past history was essentially negative. Menses started at fourteen years of age, were always normal, and her last regular period was eight months ago, June 9, 1925. She has been married twenty-five years and has had nine full-term children, all spontaneously delivered, seven of whom are living.

Her present illness started about six months after the delivery of her last baby six years ago. At that time she began to notice a weakness and clumsiness in her hands and arms which became progressively worse and later involved her lower extremities so that she became bedridden. In addition, during the past year and one-half she has partially lost the power of speech and the ability to masticate food.

This condition was diagnosed and treated by Dr. Irving Pardee, at St. Luke's Hospital, shortly after its onset. More than a year ago, however, her condition was pronounced hopeless. Nevertheless, so far as the husband has been able to observe, there has been no marked change in her condition since she became pregnant eight months ago.

Examination reveals the following: Patient is a well-developed and well-nourished woman, but whose speech is slurring and indistinct, who is unable to close her mouth or masticate food, who drools constantly, who has difficulty in swallowing, has exaggerated reflexes and who presents marked weakness and incoordination of the movements and marked muscular atrophy of the hands, arms, feet, and legs.

Abdominal examination presents a symmetrically enlarged, gravid uterus about the size of a thirty-six weeks' pregnancy. The attitude, size of the fetus, fetal

\*Read by invitation before the Obstetrical and Gynecological Section of the New York Academy of Medicine on March 26, 1929.



movements, and fetal heart were normal. Urinalysis was normal and the systolic blood pressure was 120.

The day after admission to the hospital she was seen in consultation and the diagnosis confirmed of amyotrophic lateral sclerosis with early bulbar palsy.

Inasmuch as the patient was not in labor she refused to remain in the hospital. Ten days after her discharge she was admitted to the Jewish Memorial Hospital where, after an easy labor of only two hours, she was delivered of an eight-pound normal baby. Following delivery the uterus acted normally, there was only the usual blood loss and after a normal puerperium of ten days' duration she was discharged.

For a period of six months following delivery, the husband states that his wife seemed to improve, as it was apparent that the movements of her hands and arms increased and she was more easily fed. Subsequently, however, her condition gradually became worse and she died August 5, 1928, two and one-half years after the birth of her baby.

At birth the baby was apparently healthy in every respect. Since then he has maintained perfect health, has made normal progress and at the present time is three years old and as strong and healthy as the average baby at this age.

#### DISCUSSION

Amyotrophic lateral sclerosis is a disease of the central nervous system. It does not affect the reproductive organs. There is, therefore, no reason why women with this disease who are in the childbearing period should not become pregnant. It follows, also, that the probability of these women, hopelessly paralyzed as they are, going through pregnancy uneventfully and of delivering spontaneously a healthy baby is the same as for any normal woman. The same is true of interrupting the pregnancy. This should not be done because, in itself, this procedure would be more dangerous to the mother than allowing the pregnancy to continue; because the disease always terminates fatally the continuation of the pregnancy does not affect the mother's prognosis; and finally, because the likelihood of obtaining a normal baby is probably as great as in a normal woman.

121 EAST SIXTEENTH STREET.

## REPORT OF A CASE OF KRUKENBERG'S TUMOR

By M. W. SEARIGHT, M.D., F.A.C.S., MEMPHIS, TENN.

MRS. S., aged forty-nine, was admitted to the medical service of the Baptist Memorial Hospital, March 27, 1927, complaining of pain beneath the ribs and swelling of the abdomen. The pain began two years ago. Six weeks prior to admission it was greatly exaggerated and was associated with gradual enlargement of the abdomen which had reached the proportions of a full-term pregnancy. She had practically no gastrointestinal symptoms except moderate constipation which was easily corrected by an occasional laxative. Slight dyspnea on exertion, but no orthopnea. No fever or cough but an occasional headache. Smarting pain was felt after micturition but no frequency; nocturia one to three times. Past illnesses were irrelevant except for several malarial attacks. Used coffee and snuff in rather large amounts. Menses began at age of thirteen, were of the thirty day type, not painful, three day flow. Slight diminution in amount for the last year. Had ten children, normal deliveries. No miscarriages.

The physical examination was essentially negative except for the abdomen which was markedly distended. All the signs of free fluid were present.

A working diagnosis of atrophic cirrhosis of the liver was made, and the abdomen was tapped to allow more satisfactory palpation and to relieve distention, as well as to study the character of the fluid itself. One hundred and twenty-eight ounces of bile-stained, turbid fluid were withdrawn. Following paracentesis, it was found that the liver and spleen were not palpable, but there was a large mass of firm consistency in the pelvis.

Vaginal examination confirmed the abdominal findings, and gynecologic consultation was requested. The pelvic findings were as follows: Perineum lacerated; cervix lacerated, large and fixed in the vaginal axis. The uterus was asymmetrically enlarged, nodular, and fixed in retroversion. There was a mass like a small bunch of grapes in the culdesac. The entire pelvis was tender. It was believed that we were dealing with a fibroma of the uterus complicated with adenocarcinoma, which would account for the delayed menopause and spotting, and metastasis to the peritoneum to account for the ascites. Advised exploratory incision lest the entire condition be benign, such as fibroma of the ovaries since it had lasted over a period of two years without causing appreciable cachexia.

The abdomen was opened April 12. The ovaries were found to be enlarged and nodular, about the size of small oranges. The tubes were apparently normal; the uterus was retroverted. On the left side, in the peritoneum along the brim of the pelvis were a number of small nodules similar to the ovarian tumors. A subtotal hysterectomy and bilateral salpingo-oophorectomy were done. The patient's condition did not warrant further exploration.

There was a severe postoperative reaction which necessitated the use of intravenous saline. The wound healed by first intention. On the seventh day after operation the temperature rose to 103° F., and there was tenderness over both kidneys. She was treated for pyelitis, with only slight improvement. On May 2, it was evident that the abdomen was refilling with fluid, and five days later 3000 c.c. of cloudy yellow fluid were withdrawn. The patient gradually became unable to take food of any kind. Death occurred May 15, 1927, a little more than thirty days postoperative.

*Pathologic Report.*—The specimen consisted of the uterus, amputated supravaginally with both tubes and two pale, nodular masses, which had apparently

developed from the ovaries. The larger growth measured  $10\frac{1}{2}$  by 7 by 5 cm. and weighed 237 gm. The cut surface had a greyish-yellow appearance which consisted of fibrous tissue separating areas which were soft and yellow. A few small cysts were present. The smaller mass measured 7 by  $5\frac{1}{2}$  by 5 cm., weighed 97 gm., and had the same nodular appearance as the larger mass. The cut surface had about the same appearance as the larger mass, but was somewhat denser in consistency. The uterus showed a few vascular adhesions, and there was considerable arteriosclerotic change in the wall. The mucosa was thin and leathery. Microscopically, the ovarian tumors showed small groups of large round cells with mucoid contents which compressed the nucleus into a signet ring form. These groups were surrounded by fibrous tissue.

*Diagnosis.*—Fibrosarcoma mucocellulare carcinomatodes of Krukenberg.

The ascitic fluid showed no growth in twenty-four hours. A trace of bile was present. Microscopically, there were many large endothelial cells undergoing degeneration. No mitotic figures were found. There were also many lymphocytes and a few polymorphonuclear cells. The urea-nitrogen was 11.44 mg. per 100 c.c.; the nonprotein nitrogen was 26.55. Wassermann negative. Sedimentation time to 111-12 minutes. Repeated smears for malaria were negative. White blood counts ranged from 5,300 to 11,000.

Autopsy was done May 4, 1927. Briefly the findings were as follows:

The stomach was found to be much thickened and contracted. The lesion began at the cardia and extended around the lesser curvature through the pylorus. In some places the stomach wall reached a thickness of  $2\frac{1}{2}$  cm., and was cut with considerable difficulty. The mucosa was thrown into folds and nodular elevations. It was free from ulceration. The pylorus was fixed by adhesions. The pyloric lymph nodes were enlarged, pale, and indurated. Extensions to the peritoneum had given rise to fibrous thickening, constricting the intestine, and causing marked cicatricial contraction of the omentum. The retroperitoneal glands along the course of the aorta were markedly enlarged and indurated. There were about twenty of these nodes along the superior border of the pancreas, superior surface of the diaphragm, and scattered through the mesentery. The appendix was hard and rigid, 1 cm. in diameter. The cystic duct and neck of the gall bladder were also infiltrated by extension of the growth, forming a pale rigid tube about 2 cm. in diameter. The terminal ileum was covered with dense adhesions and could not be freed. There was an abscess cavity which apparently communicated with the bladder. Both kidneys were slightly enlarged and contained multiple small abscesses. The spleen and liver were apparently negative. The peribronchial lymph glands were enlarged. The entire colon was collapsed.

Microscopic examination of the stomach revealed new tissue, chiefly in the submucosa, and the muscularis was also much thickened and traversed by opaque bands of fibrous tissue. There was a diffuse infiltration of large, granular, acidophilic, vacuolated cells with large nuclei. Glands from the superior border of the pancreas showed the gland-like arrangement of adenocarcinoma through which black pigment was scattered. The retroperitoneal, mesenteric glands and along the diaphragm were infiltrated with cancerous cells similar to those found in the stomach. The appendix had become obliterated, and the cystic duct was partially obstructed by metastatic involvement. A small node in the mesoappendix was also malignant, as well as the peribronchial nodes.

*Anatomic Diagnosis.*—Carcinomatosis, apparently primary in the stomach.

# A COMPARISON OF THE RESULTS OBTAINED IN THE INDUCTION OF LABOR BY MEANS OF BOUGIE OR BAG

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*(From the Department of Obstetrics, Johns Hopkins Hospital and University)*

## INTRODUCTION

DURING the latter part of 1927, within a few days of each other, three cases of prolapsed cord with stillborn babies occurred, after labor had been induced for toxemia by means of the Voorhees bag. These unfortunate results aroused our interest and led us to inquire whether the best interests of the patients had been served.

With this in mind, we have critically studied the results obtained in the Clinic during the past twenty years (1908-1928), when labor was induced by means of the bag or bougie respectively, in the hope that some conclusion could be reached as to which method gives the most satisfactory results.

Dr. Williams has for years contended that it was his impression that better results followed the use of the bougie for the induction of labor in pregnant women who did not present signs of antepartum bleeding, and when haste is not essential; and this study will serve to confirm or refute such a belief.

A few preliminary statements are necessary before giving actual figures. In the first place, only cases of straight induction are considered; no instance in which a bag was inserted for one reason or another *after* the onset of labor is included. Second, the cases cover all periods of pregnancy after the twentieth week, and include all indications except antepartum bleeding, due particularly to placenta previa and premature separation of the normally implanted placenta. Patients presenting these latter complications are excluded because it is felt that they present an entirely different problem.

A word should be said concerning the type and size of the bags and bougies in use in this Clinic. We use routinely the Voorhees bag, which varies in size from 5 to 10 cm. in diameter across the top; the largest bag possible is used. It may be said here that we are unable to correlate the success of the induction with the size of the bag, as in all but a few of the cases reported the largest bags were used (8 to 10 cm. in diameter). The bougie in use is the Wales bougie. This is a rubber rectal tube with a small lumen and relatively thick walls, stiff enough to be introduced without the aid of a stylet, and still soft enough to adapt itself to the contour of the uterine cavity. The sizes commonly used vary from 1.5 to 3 cm. in diameter, and it is our custom

to employ the largest size possible, or else to introduce several smaller ones. Stress is laid upon the type of bougie employed, since to most persons the term suggests the fabric structures which were formerly so generally used in urology.

Further, a word should be said concerning the method of inserting the bag or bougie. The bag is folded and made as small as possible; it is grasped by a specially constructed forceps (similar to the sponge stick forceps but different in that the blades can be disarticulated), and introduced into the uterus extraovularly whenever possible by means of a bivalve speculum or by the sense of touch alone, depending upon the preference of the operator. Upon removing the forceps the bag is completely filled with sterile saline, the hand remaining in the vagina until the operation is complete to insure that the bag remains in place. The bougie should always be inserted through a speculum, extraovularly if possible; it is inserted into the uterus for almost its entire length, 2 to 3 cm. only protruding through the cervix; the vagina is then packed with gauze to hold it in place. Both procedures are carried out without anesthesia whenever possible, particularly in cases of toxemia, and it is surprising how few patients require the administration of an anesthetic. The bag or bougie is never allowed to remain in place for longer than twenty-four hours, on account of the danger of infection.

#### THE BOUGIE

Upon analyzing our figures, it was found that an attempt was made to induce labor by means of the bougie in 160 cases, which was successful in 132 cases, or 82.5 per cent. In Table I (A) are given the indications

TABLE I (A)

INDICATIONS FOR INSERTION OF BOUGIE	MATURE 85 CASES		PREMATURE 36 CASES		IMMATURE 39 CASES		TOTAL
	SUCCESS- FUL	FAILED	SUCCESS- FUL	FAILED	SUCCESS- FUL	FAILED	
A. Nephritis and nephritic toxemia	7	1	7	5	11	2	33
B. Preeclampsia	19	1	8	0	4	0	32
C. Toxemia, low reserve kidney	7	0	5	3	3	1	19
D. Eclampsia	4	0	1	1	5	0	11
E. Tuberculosis	0	0	0	0	2	3	5
F. Cardiac	3	0	2	0	2	1	8
G. Prolonged pregnancy, excessive size of child, disproportion	29	7	0	0	0	0	36
H. Pyelitis	0	0	2	0	2	0	4
I. Miscellaneous: hydram- nios, dead fetus, cancer, neuritis, psychosis, missed abortion, chole- lithiasis	6	1	1	1	2	1	12
Totals	75	10	26	10	31	8	169
Efficiency	88.2%		79.2%		79.5%		82.5%

for which the inductions were attempted. From it, will be seen that the cases are divided into three groups, patients at or near term (with fetus weighing 2500 gm. or more), patients with premature babies (weighing 1500 to 2500 gm.), and patients with immature or nonviable babies (weighing less than 1500 gm.). The number of successful and unsuccessful cases are given for each group. As might be expected, the bougie was most efficient in the first group, the percentage of success being 88.2. On the other hand, it was less efficient in the other two groups, in which the results were negative in about one case in five.

In the great majority of cases the main indications were toxemia and prolonged pregnancy, the percentage of success being 87.1 for the former, and 80.6 for the latter.

Of the 132 cases in which labor followed the insertion of the bougie 96 were delivered spontaneously, a percentage of 72.7. But when we figure the percentage of total number of inductions attempted which finally delivered spontaneously the figure falls to 59.6 per cent, which represents the expectancy of spontaneous delivery when we set out to induce labor by means of the bougie. In the 27 per cent of cases which did not end spontaneously, labor was terminated by forceps, version and extraction, and occasionally by craniotomy, depending upon the indication.

#### FETAL MORTALITY

Deducting 33 cases in which the fetus was dead or nonviable at the time of insertion of the bougie, there remain 99 cases on which to figure the fetal mortality. In this group there were 16 stillborn babies, and 2 babies who died a few hours later, a total of 18. Ten of the 18 deaths occurred in cases ending spontaneously, and 8 in those ended by supplementary operation. One of the 8 operations was done for prolapsed cord, and in three other cases, the operation must be held re-

TABLE I (B). FETAL DEATHS

TYPE OF CASE OR CAUSE OF FETAL DEATH	MATURE 85 CASES	PREMATURE 36 CASES	IMMATURE 39 CASES	TOTAL
Prolapsed cord	2	0		2
Eclampsia	2	1		3
Preeclampsia	2	1		3
Nephritis	0	5		5
Cardiac	0	1		1
Unexplained	1	0		1
Totals	7	8		15
Mortality	9.3%	32%		15.06%
Killed by operation	3	0		3
Dead or nonviable	2	1	30	33

TABLE I (C). MATERNAL RESULTS

Morbid	18	10	9	37
Dead	1	1	2	4

sponsible for the death of the baby; in two of them craniotomy was done after failure of forceps or version. The remaining 4 operations were incidental, such as low forceps.

Reference to Table I (B) will show the cause of the fetal death, and the type of case in which it occurred. Obviously, all the fetal deaths are not attributable to the method of induction employed. Thus, if we exclude the 3 cases in which operation was responsible for the fetal death the mortality is 15.06 per cent, but if we exclude the toxemias as well, the mortality falls to 4 per cent. The fetal mortality for the mature group is only 9.3 per cent as compared with 32 per cent for the premature group. All but one of the fetal deaths in the latter group occurred in cases of severe toxemia or nephritis, a consideration which shows what large factors toxemia and prematurity are in the production of fetal mortality.

#### MATERNAL MORBIDITY AND MORTALITY

Thirty-seven of the 132 cases had febrile puerperia, but as three of them showed signs of infection at the beginning of the induction they must be deducted in calculating the maternal morbidity (a rise to 100.4° F. or more on any two days after the first). Furthermore, the fact that the temperatures are taken every four hours increases the rate of morbidity considerably. The maternal morbidity is thus 18.6 per cent.

There were 4 maternal deaths. One patient died of subacute bacterial endocarditis (Unit 3950) and one of uremia (Service No. 8043), so that neither of them can fairly be called obstetric deaths. Of the other two, one died of a gas bacillus endometritis, and the other suffered a ruptured uterus, later dying of peritonitis.

Clinic No. 8797½, F. H. The patient was a colored multipara, aged forty-two, whose last menstrual period occurred on Feb. 15, 1917. She had been followed in the Dispensary for about six weeks before admission to the hospital. When first seen she presented signs of severe toxemia of pregnancy, with blood pressure 210/120, albumin 2+, marked edema of the extremities, and complaining of occasional severe headache. She was advised to enter the hospital, but refused to do so. She was seen on several occasions thereafter, the signs and symptoms of the toxemia being a little worse at each successive visit. Finally a few days before admission she began to have epigastric pain, to be nauseated and to vomit; the fetal movements ceased; dimness of vision appeared; the patient became alarmed and entered the hospital Sept. 27, 1917, when the blood pressure was 190/100, and the urine contained many casts and 4 gm. of albumin per liter. The uterus corresponded in size to an eight months' gestation, and the temperature was normal. On September 29, after failure to induce labor by means of castor oil and quinine, a bougie was inserted, and an 1800 gm. macerated fetus possessing an exceedingly foul odor was born fifteen hours later. The toxemia immediately improved, but on the day following delivery the temperature rose to 100.4, pulse 110; and from then onward the temperature and pulse remained elevated, with occasional remissions. The patient seemed well until October 4, when she began to act queerly, refusing to see her relatives. She gradually became stuporous, her urine was

bloody and contained pus, there appeared a conjugate deviation of the eyes, and she could not be aroused. The stupor gradually increased until she died a few hours later. At autopsy it was found that she had an acute endometritis, thrombosis of the innominate vein and right carotid artery, beginning arteriosclerosis, myocardial degeneration and edema of the lungs. Cultures of the uterine contents grew out gas bacillus, *Staphylococcus aureus*, and *Bacillus coli*.

The second case which resulted in death was as follows. Clinic No. 11,375, M. O. The patient was a colored woman, aged thirty-four, whose single previous pregnancy had ended in spontaneous abortion at three months. She was admitted to the hospital on Sept. 22, 1921, about six and one-half to seven months pregnant, with a history of increasing symptoms of toxemia for six weeks. On that morning, she awoke with severe headache, epigastric distress, and dimness of vision. Twenty minutes after admission she had a third and last convulsion. Venesection and hot packs brought about temporary improvement. Two days later because of rising blood pressure it was decided to induce labor by means of the bougie. The cervix was found to be tightly closed; it was dilated with the Goodell dilator before the bougie could be inserted. Ineffectual pains ensued after a few hours. On the following day, the bougie was removed and a bag introduced in order to hasten labor. The temperature at this time was 102° F. A 1120 gm. macerated fetus was expelled after seven hours. Four days later the toxemia was much improved, but the temperature and pulse remained elevated and continued so until death occurred on the eighth day. Autopsy revealed a rupture of the lower uterine segment into the left broad ligament, which contained a sizable abscess cavity, which again had ruptured into the peritoneum, leading to a generalized peritonitis. A note by Dr. Williams at the time suggests the Goodell dilator as being the probable cause of the ruptured lower segment. Additional findings at autopsy were subacute nephritis, moderate anasarca, cloudy swelling of liver and spleen.

These two deaths must obviously be laid to the insertion of the bougie, and constitute a maternal mortality of 1.3 per cent. See Table I (C).

#### PROLAPSED CORD

In the bougie inductions prolapse of the cord occurred six times, an incidence of 4.5 per cent. In two instances the child was nonviable, in two others live children were born in spite of the prolapsed cord. In the remaining two cases, the membranes had been ruptured accidentally before the cervix became fully dilated. In one case this occurred when the bougie was inserted, while in the other it occurred when a bag was inserted to hasten dilatation when the cervix was 4 cm.; both babies were stillborn. In other words, two of the 18 fetal deaths were really attributable to prolapsed cord following early rupture of the membranes.

#### MEMBRANES

An attempt was made to correlate the occurrence of prolapse of the cord and febrile puerperia with the time at which the membranes ruptured. Table II presents an analysis of our findings with these points in mind. It shows that accidental rupture of the membranes occurred 16 times, or in 12 per cent of the cases; while in 3 others the membranes were ruptured intentionally before the cervix had become fully dilated



in the hope of hastening the course of labor. In this group of 19 cases, 3 of the 6 prolapsed cords occurred, and these included the two instances in which the children were stillborn.

TABLE II. BOUGIE. CORRELATION OF PROLAPSE OF THE CORD AND THE FEBRILE PUERPERIA WITH THE TIME OF RUPTURE OF THE MEMBRANES

TIME OF RUPTURE	CASES	PROLAPSED CORD	STILL-BORN	DEAD OR NONVIABLE	FEBRILE PUERPERIA
1. Before insertion of bougie	2	0	1	0	2
2. At insertion of bougie	16	2	1	3	2
3. Artificially before full dilatation	3	1	1	2	0
4. In course, at or after full dilatation, at operation	94	1	12	23	27
5. Unknown	17	2	3	5	6
Totals	132	6	18	33	37

Contrary to our expectations the great majority of febrile puerperia occurred in two rather unspecific groups; namely, in that in which the time of rupture of the membranes was unknown (5), and in group 4 in which the membranes had ruptured spontaneously during the course of labor, or had been ruptured artificially after full cervical dilatation. Naturally, when rupture of the membranes occurred at insertion of the bougie, it was accidental; but obviously, such an accident must increase the likelihood of prolapse of the cord and of fetal death.

#### TIME REQUIRED FOR INDUCTION AND DURATION OF LABOR

Table III shows the length of time elapsing between the introduction of the bougie and the onset of labor, as well as the duration of labor after the pains have begun.

TABLE III. BOUGIE

	TIME FOR INDUCTION			DURATION OF LABOR		
	MULTIP- ARAE	PRIMI- PARAE	TOTAL	HOURS	AVERAGE	
1. Immediate or in less than one hour	12	6	18	1. Operative	18.2	
2. Average time for others (hours)	5.95	6.85	6.4	2. Spontaneous	12.4	
				3. Multiparae	11.3	
				4. Primiparae	17.1	14.2

It will be noticed that pains set in within the first hour in 14 per cent of the cases, while on the other hand this did not occur until after the lapse of twenty-four hours in other cases. The average for the entire number of cases was six and four-tenths hours, leaving out of account the cases in which the induction failed entirely. Furthermore, it should be remembered that it is our practice never to allow the bougie to remain in place for more than twenty-four hours.

The average duration of labor was fourteen and two-tenths hours. The primiparous labors were six hours longer than the multiparous, a difference which corresponds to that usually stated in textbooks. On

the other hand, the operative labors were six hours longer than the spontaneous deliveries, which is due to the fact that these patients were allowed to continue in labor until some definite indication for interference arose.

#### THE BAG

A bag was inserted in the attempt to induce labor in 49 cases, and was successful in 46, an efficiency of 93.8 per cent. It is noteworthy that the three failures occurred in patients in whom a bougie had previously been inserted and had failed to bring about the onset of labor. Twenty-seven of the 46 successful cases ended in spontaneous delivery, a percentage of 58.8. As 27 is 55.1 per cent of 49 (the total number of inductions attempted), this figure must be regarded as representing the expectancy of spontaneous delivery when the bag is used.

In Table IV (A) are detailed the successes and failures occurring under each of the various indications, and these are again divided according

TABLE IV (A)

INDICATIONS FOR INSERTION OF BAG	MATURE 24 CASES		PREMATURE 18 CASES		IMMATURE 7 CASES		TOTAL
	SUCCESS- FUL	FAILED	SUCCESS- FUL	FAILED	SUCCESS- FUL	FAILED	
A. Failure of bougie	4	1	6	1	3	1	16
B. Preeclampsia	0	0	1	0	0	0	1
C. Toxemia, low reserve kidney	1	0	0	0	0	0	1
D. Eclampsia	4	0	3	0	1	0	8
E. Tuberculosis	1	0	0	0	0	0	1
F. Nephritis and nephritic toxemia	4	0	4	0	1	0	9
G. Pyelitis	0	0	0	0	1	0	1
H. Diabetes	1	0	0	0	0	0	1
I. Prolonged pregnancy, excessive size of child, etc.	7	0	0	0	0	0	7
J. Miscellaneous, intra- partum infection, ab- normal presentation, anemia	1	0	3	0	0	0	4
Totals	23	1	17	1	6	1	49
Efficiency	95.8%		94.4%		85.7%		93.8%

as the pregnancy was mature, premature, or immature. As was to be expected, the efficiency of the method was found to be greater in the mature and premature groups, the percentage of success being 95 per cent for the former two as compared with 85 per cent for the latter. The number of cases is small and therefore such figures cannot be regarded as absolute.

As will be noted the various types of toxemia constituted the most common indication, and in the 19 cases there were no failures. The next indication was failure to induce labor by means of the bougie, 16 cases with 3 failures; while the only other indication of considerable

frequency was prolonged pregnancy of which there were 7 cases, all successful.

#### FETAL MORTALITY

In 14 instances the fetus was dead or nonviable at the time of insertion of the bag, thus leaving 32 cases upon which to calculate the fetal mortality; and in these, 12 children were stillborn and three died shortly after delivery. Of the 15, 5 were born spontaneously and 10 by operative means. Four of the 10 operations were necessitated by prolapse of the cord, while in 5 other cases the child died during the course of the operative procedure (version and extraction 3, midforceps 1, breech extraction 1).

TABLE IV (B). FETAL DEATHS

CAUSE OF FETAL DEATH OR TYPE OF CASE	MATURE 24 CASES	PREMATURE 18 CASES	IMMATURE 7 CASES	TOTAL
Prolapsed cord	4	2		6
Eclampsia	1	1		2
Nephritis	1	1		2
Total	6	4		10
Mortality	26.1%	23.5%		31.2%
Killed by operation	2	3		5
Dead or nonviable	4	3	7	14

TABLE IV (C). MATERNAL RESULTS

Morbid	7	9	2	18
Died	0	1	0	1

Table IV (B) shows in detail the cause of the fetal death and the type of case in which it occurred. Deducting operative mortality, the fetal mortality is 31.2 per cent. If we deduct the toxemias as well, this falls to 18.7 per cent, and there is some justification for so doing, because only the 6 deaths due to prolapse of the cord can be directly attributed to the method of induction. The fetal mortality for the premature group is slightly less than for the mature group, 23.5 and 26.1 per cent respectively, which is explained by the fact that 4 of the 6 fetal deaths from prolapsed cord fell in the latter group.

#### MATERNAL MORBIDITY AND MORTALITY

In 18 cases, the puerperium was febrile, not including the cases in which intrapartum infection afforded the indication for interference, so that the maternal morbidity is 37.7 per cent. If we correlate the morbidity with the number of manipulations, it is very graphically shown that the greater the number of the latter, the higher becomes the incidence of infection (Table VII). There was one maternal death from peritonitis following vaginal hysterotomy after both bougie and bag had failed to complete the labor (U. 3762), giving a maternal mortality of 2.1 per cent.

## PROLAPSED CORD

The cord prolapsed in 8 cases, an incidence of 17.4 per cent, and in 6 of these the child was stillborn. In 5 cases in this group the membranes were ruptured accidentally at the time of insertion of the bag; in another case they had ruptured prematurely before the induction was begun; while in the remaining two they were ruptured artificially by the obstetrician during the course of labor, before full dilatation. Incidentally it might be said that 4 of the 6 stillbirths probably resulted from the operative procedures undertaken in the hope of saving the child.

## MEMBRANES

As in the case of the bougie, an attempt was made to correlate prolapse of the cord and febrile puerperia with the time of rupture of the membranes. Table V shows several remarkable facts: the membranes were

TABLE V. BAG. CORRELATION OF PROLAPSE OF THE CORD AND THE FEBRILE PUERPERIA WITH THE TIME OF RUPTURE OF THE MEMBRANES

TIME OF RUPTURE	CASES	PROLAPSED CORD	STILL-BORN	DEAD OR NONVIALE	FEBRILE PUERPERIA
1. Before insertion of bougie	5	1	2	1	2
2. At insertion of bougie	2	2	2	0	1
3. At insertion of bag	14	3	6	3	7
4. Artificially before full dilatation	3	1	2	0	3
5. In course, at or after full dilatation, at operation	18	1	3	6	3
6. Unknown	4	0	0	4	2
Totals	46	8	15	14	18

ruptured accidentally at the insertion of the bougie or bag in 16 cases, while in 3 others the membranes were ruptured purposely before full dilatation in the hope of hastening the course of labor. In this group of 19 cases (41.3 per cent of the total number of successful inductions), fall 11 of the 18 febrile puerperia, 6 of the 8 prolapsed cords, and 6 of the 8 stillbirths. These figures show conclusively how extraordinarily serious it is to rupture the membranes before full dilatation when the bag is employed, although it must be appreciated that in many cases it is often extremely difficult to insert a bag without rupturing them.

## TIME REQUIRED FOR INDUCTION AND DURATION OF LABOR

The figures in Table VI show the time elapsing between the insertion of the bag and the onset of labor, as well as the average duration of

TABLE VI. BAG

	TIME FOR INDUCTION			DURATION OF LABOR		
	MULTIPARAE	PRIMIPARAE	TOTAL		HOURS	AVERAGE
1. Immediate or in less than one hour	15	9	24	1. Operative	14.3	
2. Average time for others (hours)	5.14	4.53	4.42	2. Spontaneous	8.1	
				3. Multiparae	8.3	
				4. Primiparae	14.2	11.72

TABLE VII. BAG. SHOWING THE RELATION OF MATERNAL MORBIDITY TO INTRAUTERINE MANIPULATIONS

	AFEBRILE	FEBRILE	TOTAL
One manipulation	16	5	21
Two or more manipulations	11	12	23
Excluding 2 cases of intrapartum infection			44

labor. It is seen that pains set in in less than one hour after the insertion of the bag in approximately 50 per cent of the cases, while in the other half the average time was four and forty-two hundredth hours, although as long as twenty hours was required on several occasions. The duration of labor was from three to four hours shorter than when the bougie was used, although the difference in the duration of the multiparous and primiparous labors, as well as the spontaneous and operative labors remained essentially the same.

## COMPARISON OF THE TWO METHODS

In Table VIII the results of the two methods are compared in detail.

TABLE VIII. COMPARISON OF THE TWO METHODS

	BOUGIE		BAG	
	CASES	PER CENT	CASES	PER CENT
<i>General</i>				
1. Total number of cases	160		49	
2. Successful cases	132	82.5	46	93.8
3. Spontaneous delivery	96	72.7	27	58.8
4. Expectancy of spontaneous delivery		59.6		55.1
5. Breech presentation	3	2.3	7	15.2
<i>Fetal Mortality</i>				
1. Gross mortality	18	18.1	15	46.9
2. Mortality minus operative mortality	15	15.06	10	31.2
3. Mortality minus operative and toxemia mortality	4	4.0	6	18.7
<i>Maternal Morbidity and Mortality</i>				
1. Morbidity	34	18.6	17	37.7
2. Mortality, obstetric	2	1.3	1	2.1
<i>Prolapsed Cord</i>				
1. Total number, incidence	6	4.5	8	17.4
2. Stillborn babies	2		6	
<i>Rupture of Membranes</i>				
1. Accoucheur responsible	19	14.4	19	41.3
2. Prolapsed cords in this group	3	50.0	6	75.0
3. Stillborn in this group	2	13.3	8	80.0
4. Febrile puerperia in this group	2	5.4	11	64.7

The following points are deserving of comment: The bag was the more efficient of the two methods, though by not a great deal, 93.8 per cent as compared with 82.5 per cent. On the other hand, it appears that a considerable point in favor of the bougie is the much greater percentage of spontaneous delivery (72.7 per cent and 58.8 per cent). Even when

the greater proportion of failures following attempted induction by means of the bougie is taken into consideration, it appears that the actual expectancy of spontaneous labor is still a trifle greater than with the bag (59.6 and 55.1 per cent).

The fetal results are distinctly in favor of the bougie, although neither method gives ideal results. The mortality for bag induction, considering gross fetal mortality, minus the operative mortality, as being the fairest estimate, was twice as great as with the bougie. Likewise the maternal morbidity was twice as great for the bag as for the bougie while the maternal mortality was essentially the same. On the other hand, the relative incidence of prolapse of the cord was four times greater with the bag than with the bougie.

Prolapsed cord, it is seen, was responsible for all the fetal deaths directly attributable to the method in the bag group, as compared with only one-half the fetal deaths in the bougie group. Obviously in both groups, early rupture of the membranes before full dilatation, at the insertion of either bougie or bag, or when done artificially later on, proved disastrous from all points of view. Particularly is this true for the bag, in which 75 per cent of the prolapsed cords, 80 per cent of the fetal deaths, and 64.7 per cent of the febrile puerperia followed too early rupture of the membranes. Moreover, it is shown clearly that the chance of rupturing the membranes at the time of insertion is much greater with the bag than with the bougie (34.7 per cent as compared with 12 per cent). This in itself is a considerable argument against the bag, especially in view of the results obtained in this particular group of cases. Finally, labor set in immediately after the insertion of the bag many times more frequently than after the bougie, and the time elapsing before the onset of pains, as well as the actual duration of labor, was definitely shorter.

It is an interesting commentary that the incidence of breech presentations was 15.2 per cent in the cases induced by the bag as compared with 2.3 per cent for the bougie group.

#### CONCLUSIONS

1. Our study shows that the bougie is superior to the bag for the induction of labor, provided a sufficiently large bougie is employed, and that it should be used whenever haste is not essential.
2. The bag is more efficient in bringing about the onset of labor, but is attended by a definitely greater fetal mortality and maternal morbidity.
3. When fetal death follows the use of the bag it is usually the result of prolapse of the cord.
4. The maternal mortality is the same with either method.

# COMPLETE ATRESIA OF THE CERVICAL CANAL DURING PREGNANCY AS A COMPLICATION OF CERVICAL HYPERTROPHY

WITH THE REPORT OF A CASE

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COMPLETE atresia of the cervical canal during pregnancy as a complication of cervical hypertrophy is extremely rare. Of all the parturients admitted to the Philippine General Hospital from 1910 to 1928 (18,274 cases), only the case here reported presented this complication.

In the literature to date, which had been reviewed by Mathieu and Schaufler, only 27 cases of cesarean section were performed on account of cervical atresia and of these 6 were cases of obliteration of the cervical canal.

B. J., aged twenty-nine, para iv, was admitted to the Philippine General Hospital on September 24, 1928, in her ninth month of pregnancy. Previous labors were all prolonged and difficult, the first resulting in the spontaneous birth of an asphyxiated baby which soon died, and the second and third terminating in spontaneous stillbirths. Patient entered the hospital for delivery on account of previous difficult labors.

On investigating the possible cause of dystocia, the pelvic measurements were found to be normal but the vagina was occupied by a soft elongated tumor as large as a grapefruit which on closer examination was identified to be the cervix itself. The tumor was smooth and solid throughout its extent and only after careful search was a slight indentation felt on its upper and anterior right portion, which was taken to be the external os. With some effort it was made to admit a very fine probe 1 mm. in diameter as far as 1 cm. deep. This was followed however by much bleeding which made us wonder if the opening was not made artificially by the instrument. A Porro cesarean section was decided upon to be performed as soon as labor pains began. The patient however insisted on going home promising to return as soon as she felt labor pains.

On the twelfth day after examination, she returned with strong labor pains and with a temperature of 39° C. The cervical tumor had greatly increased in size so that while a large portion of it was still within the vaginal canal, a great deal of it had protruded outside the vulva. A Porro cesarean section was quickly performed under general anesthesia, but unfortunately the baby was found to be macerated. Total hysterectomy would have done away with the cervical tumor but as it was exposed to infection, it was thought safer to leave the cervix in situ.

During the first four days the vulvar pad was dry and free from any lochial secretion, but on the fifth day it was noticed to be stained with a slight sero-sanguinous discharge which gradually became whitish and increased in amount as the puerperium advanced.

During the puerperium the cervical tumor had shrunk considerably but it was still large enough to require amputation. On the eighteenth day, under spinal

anesthesia, the elongated portion beyond the tear, which was reduced to one inch long and three-fourths inch thick, was amputated and the remaining stump sutured, thus restoring the normal contour of the cervix as far as possible. Perineorrhaphy was also done. With the exception of a rise of temperature to 38° C. from the second to the fourth day, recovery was uneventful.

#### COMMENT

Various conditions have been described as the etiologic factors of cervical obstruction or occlusion. They are: (a) injury to the cervix

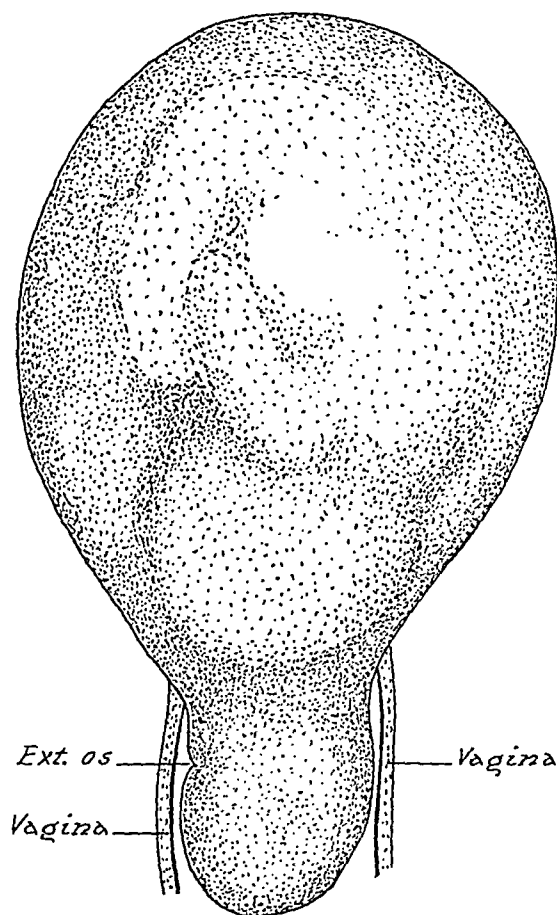


Fig. 1.—Diagrammatic view of the cervical tumor.

due to childbirth; (b) operations on the cervix such as dilatation and curettage, and trachelorrhaphy or high amputation of the cervix; (c) use of caustics in the treatment of cervical disease; (d) syphilis or chancre; (e) overlapping of the cervical lips; (f) faulty presentation unequally dilating the cervix; and (g) adhesions between the unruptured membranes and the cervical wall.

Of the above, only the first condition, namely, injury to the cervix caused by a previous labor was present in our case. Fig. 1 is a schematic drawing made of the condition of the cervix before the operation.

As to the modus operandi of the obliteration of the cervical canal. The



diagnosis of absolute occlusion of the cervical canal during pregnancy is at first disconcerting and incredible for one naturally questions that if such an obstruction really existed how could the woman have become impregnated?

The facts in our case are as follows:

1. There was complete occlusion of the cervical canal during the ninth month of pregnancy (when the patient was first seen), and throughout labor and early puerperium as proved by negative digital, ocular and instrumental tests and by the absence of lochia during the first four days of puerperium.

2. Concomitant with the occlusion was the large cervical tumor which distended and occupied most of the vaginal canal.

3. On the fifth day of puerperium, when the cervical tumor had much decreased in size for the first time, serosanguinous discharge began to appear, showing the patency of the cervical canal.

The foregoing facts lead us to explain that the occlusion of the cervical canal which developed after impregnation was not caused by any organic change in the canal itself but rather by the overgrowth of the surrounding tissue, which had reached its abnormal state under the stimulating influence of pregnancy. Once the gravid state had passed and the process of involution had fairly inaugurated itself with consequent recession of the hypertrophied cervical tissue, the patency of the canal became reestablished.

As to the method of delivery in cases of cervical occlusion or marked atresia where drainage through the cervical canal is nil or at most ineffective, it is believed that a Porro cesarean section at full term is the operation of choice, consistent with the welfare of both mother and fetus. Vaginal cesarean section should be confined only to cases of partial stenosis where the cervical canal admits two or more fingers and no tumor obstructs the pelvic canal.

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# SEASONAL VARIATION IN THE WEIGHT LOSS OF NEWBORNS

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THIS study was undertaken to determine the influence of season of the year on the weight loss and the occurrence of fever in newborns. The data were obtained from the records of several thousand infants born at Bellevue Hospital over a period of years.\*

## SEASONAL VARIATION IN THE WEIGHT LOSS

The weight loss in newborn infants during the years 1926 and 1927 by months of the year and by sex is shown in Table I and Chart 1. Each curve is based on data obtained from over fifteen hundred in-

TABLE I. SEASONAL VARIATION IN THE WEIGHT LOSS OF NEWBORNS. BELLEVUE HOSPITAL 1926 AND 1927

MONTH OF YEAR	MALES			FEMALES		
	NO. OF BIRTHS	PERCENTAGE WEIGHT LOSS MEAN	P.E.M.*	NO. OF BIRTHS	PERCENTAGE WEIGHT LOSS MEAN	P.E.M.
January	123	8.57	0.22	138	9.09	0.17
February	118	9.17	0.22	149	8.76	0.17
March	148	8.76	0.18	136	8.34	0.19
April	136	8.15	0.18	119	9.16	0.20
May	138	8.40	0.19	155	8.25	0.18
June	136	7.82	0.18	139	8.00	0.20
July	156	7.48	0.15	140	7.75	0.18
August	184	7.53	0.16	127	7.24	0.15
September	127	7.50	0.18	153	7.56	0.17
October	157	8.10	0.15	131	7.95	0.17
November	141	8.78	0.19	103	7.90	0.21
December	144	7.74	0.14	117	7.94	0.19

\*P. E. can be obtained by multiplying P.E.M. by the square root of the number of cases.

infants. The weight loss in both boys and girls born at Bellevue Hospital is considerably less during the summer than during the winter. This seasonal variation is constantly present for both years and for both sexes. The weight loss begins to diminish in June, remains low during the summer months and starts to rise in October. The weight loss during the summer months was about 15 per cent less than during the winter months, the loss during the summer months (July, August, and September) for both males and females averaging about 7.50 per

\*These studies were made possible through the courtesy and cooperation of Dr. Frederick W. Rice and Dr. Hervey C. Williamson, to whom we wish to express our sincere appreciation.

cent of the birth weight, while during the winter months (January, February, and March) the average was about 8.78 per cent.

Since a relationship exists between the loss of weight in newborns and the birth weight, the heavier babies losing proportionally more than the smaller ones, the average birth weight for this series of infants was computed for each month during the years 1926 and 1927.

Adersen<sup>1</sup> noted a seasonal variation in the birth weight, the newborns being larger during the cold weather. Hansen<sup>2</sup> found that newborns were heavier during the fall than during the spring months. According to Abel<sup>3</sup> newborns in Vienna, during the years following the war, weighed more during the summer than during the winter.

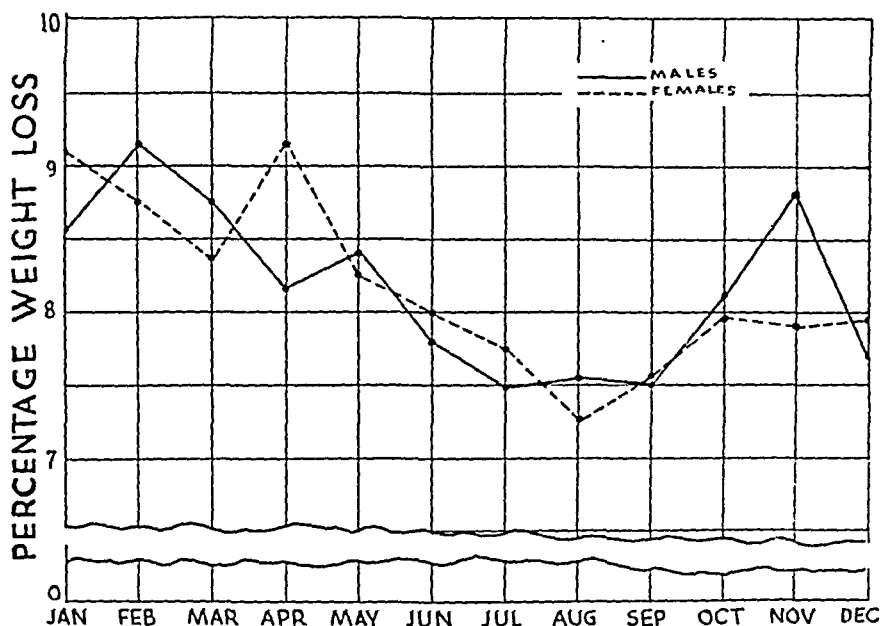


Chart 1.—Seasonal variation in weight loss of newborn infants, Bellevue Hospital, 1926, and 1927.

Brenton,<sup>4</sup> and more recently Hellmuth,<sup>5</sup> however, have been unable to find any seasonal variation in birth weight. In our series there was no constant seasonal fluctuation in the birth weight.

#### SEASONAL VARIATION IN FEVER

Adair and Stewart<sup>6</sup> in a study made at the Swedish Hospital, Minneapolis, found that during the year 1921 there was a seasonal variation in the incidence of fever in newborns, the cases being much more frequent during the summer than during the winter. The summer of 1921 in Minneapolis, according to local weather bureau reports, was unusually warm, the external temperature at times ranging between 91° and 99° F. They suggested that high external temperatures have an influence on the frequency with which fever occurs in newborns. Tyson<sup>7</sup> studied the incidence of fever in newborns at three hospitals in Philadelphia. He states that no regular seasonal variation occurred. His composite curve for the frequency of fever in the three hospitals,

however, as well as the individual curves, shows a lower incidence of fever during August and September than during the other months.

The incidence of fever (temperature of  $37.8^{\circ}$  C. and above) in newborns at Bellevue Hospital by months of the year and by sex during the years 1925, 1926, and 1927 is shown in Table II and Chart 2. As one might be led to expect from the seasonal variation in the weight loss, there is a marked seasonal variation in the incidence of fever, the cases occurring much more frequently during the winter than during the summer months. The incidence of fever starts to diminish in May, is low during June, July, and August, and starts to increase during September. Whereas the percentage of babies having fever during the

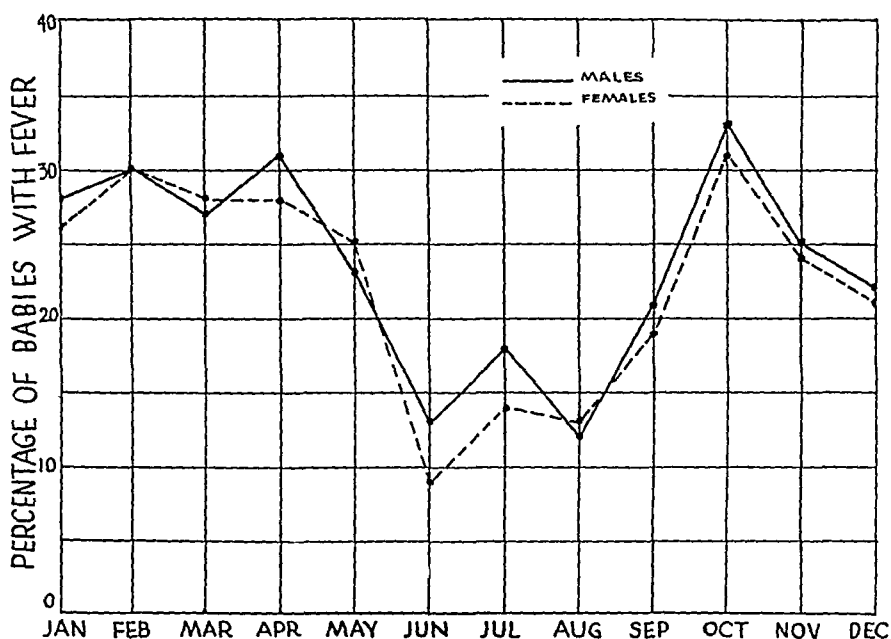


Chart 2.—Seasonal variation in the incidence of fever, Bellevue Hospital, 1925, 1926, and 1927.

winter months was usually between 25 and 30, the percentage of cases during the summer was usually below 15.

No determinable seasonal variations in the nursing care or in the water administration to newborns such as might influence the weight loss and incidence of fever were found.

In order to study the influence of temperature, humidity, etc., of the nursery on the weight loss, dry and wet bulb temperature readings were made in the newborn nursery at two-hour intervals over a period of seven months. During this period the weight loss during the first four days of life was studied in about 900 babies. The temperature range of the nursery was between  $22$  and  $29^{\circ}$  C. ( $72$  and  $84^{\circ}$  F.), the effective temperature range<sup>s</sup> between  $18$  and  $25^{\circ}$  C. ( $67$  and  $76.5^{\circ}$  F.), the humidity range from 30 to 53, and the wet bulb depression from 11 to 19.5. No correlation was found between the weight loss on any



of the first four days of life and the nursery temperature, the humidity, the effective temperature, or the wet bulb depression.

Possibly the seasonal variations in weight loss and incidence of fever are due to seasonal variations in the secretion of colostrum.

#### SUMMARY AND CONCLUSIONS

1. A seasonal variation was noted in the weight loss and incidence of fever in newborn infants kept in a nursery at Bellevue Hospital. The infants lose considerably more during the winter than during the summer and have fever more often.

2. No correlation was found between the weight loss during the first four days of life and the nursery temperature, humidity, effective temperature, or wet bulb depression.

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Levy-Solal, Misrachi, & Solomon: The Pathogenesis of the Pyelonephritides of Pregnancy. La Presse Médicale, 577, May 7, 1927.

The authors noticed the frequency of stenoses and ureteral obstructions in the course of treatment of pyelonephritis of pregnancy by ureteral catheterization. They also observed that the renal pelves showed retention to a greater extent than is found in the pyelonephritis of the nonpregnant. They determined to study their cases roentgenologically. The five cases reported are illustrative of various types of ureteropelvic abnormalities (dilatation, stricture, etc.), which malformations were evidently of long standing. Some of these anomalies (e.g., marked dilatation of the entire excretory apparatus) were classed as congenital. Hence, the theories of ureteral compression, elongation, torsion, kinking, etc., due to the pregnant uterus, are, they believe, untenable; the compression theory, for example, fails to explain the pyelonephritis of early pregnancy.

The writers call attention to the fact that bacilluria without pyelitis or pyelonephritis is common in pregnancy, and they feel that the bacilluria so frequently found after the eighth month is usually dependent upon stasis in the cecum and ascending colon. When defective renal drainage complicates the picture, pyelonephritis results; otherwise, it does not develop. They do not presume to claim, on the basis of these preliminary observations, that preexisting anatomic malformations are constant in this condition but wish to call attention to their frequency.

E. L. KING.

# VAGINAL EXAMINATION IN THE THIRD STAGE OF LABOR AS A GUIDE TO ITS MANAGEMENT\*

A STUDY BASED ON ONE THOUSAND CASES

BY MORRIS LEFF, M.D., NEW YORK, N. Y.

THE third stage of labor has been the subject of a good deal of controversy since the days of Credé, Ahlfeld, Schultze and Duncan. Their opinions have been accepted and little knowledge has since been added.

The third stage of labor remains the most dangerous of the three and (according to DeLee) "more women die from accidents of the third stage than during the other two stages combined."

In order to determine what really takes place after the baby is born, I have been making vaginal examinations in the third stage of labor, and found that my observations are radically different from the accepted theories.

At present we are guided in the management of the third stage by indirect or external signs. That is, we determine when the placenta has separated by signs not directly referable to the placenta, but rather to the lower abdomen, uterus, or cord. These supposed signs do not indicate when the placenta actually separates but rather are phenomena that occur relatively long after the placenta has already separated.

By depending on these accepted signs, it has been assumed that it takes the placenta between ten and forty-five minutes to separate; and that it is therefore necessary to wait that length of time before attempting to express it.

By making a vaginal examination soon after the baby is born, I found that the placenta separates promptly after the baby leaves the uterus. I have observed this fact in over 2500 patients delivered in the last four years.

I present here a series of 1000 consecutive cases (exclusive of cesarean sections and placenta previa centralis) delivered between January 1, 1927, and July 1, 1928, in which vaginal examinations had been made to determine the separation of the placenta.

Table I gives the time of the delivery of the placenta. It shows that in 878 cases the placenta was delivered within five minutes after the birth of the child. In 98 cases within ten minutes, and in only 24 cases did it take more than ten minutes. In only 2 cases was manual removal of the placenta necessary. The average time for the delivery of the placenta in these 1000 cases was four and three-tenths minutes. The fact that these placentas had separated and were delivered in this short

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\*Read at a meeting of the Section of Obstetrics and Gynecology of the New York Academy of Medicine, Dec. 18, 1928.

period goes to disprove the accepted view that it takes between ten and forty-five minutes for the placenta to separate.

The retroplacental hematoma is given in most textbooks as a factor in causing the separation of the placenta. Some authors emphasize its importance and caution against disturbing it for fear of interfering with the proper separation of the placenta. I do not believe that the

TABLE I. TIME OF DELIVERY OF PLACENTA AFTER THE BIRTH OF CHILD

MINUTES	NO. OF CASES	
0	4	
2	190	
3	368	
4	133	
5	183	878
6	13	
7	41	
8	8	
9	3	
10	33	98
11	2	
12	4	
15	7	
17	2	
18	1	
20	2	
22	1	
25	1	
35	1	
65	1	Manual removal
85	1	Manual removal
90	1	24
		1000

Average time four and three-tenths minutes.

retroplacental hematoma is a factor in the separation. It takes no part in the mechanism, but rather is produced as a result of the separation. The hematoma becomes larger the longer the placenta remains in the uterus, and prevents the uterus from contracting properly.

In the Duncan method of placental extrusion, it is evident that the hematoma cannot exert any influence in the separation, as the blood escapes through the cervix and vagina. On the other hand in the Schultze mechanism the blood is retained not because it is necessary for

TABLE II. BLEEDING BEFORE AND AFTER DELIVERY OF PLACENTA

DESIGNATION	OUNCES	NO. OF CASES
Very slight	0 - 3	134
Slight	3 - 6	578
Moderate	6 - 12	243
Considerable	12 - 20	41
Profuse	20 and over	4
		1000



the separation of the placenta but because it cannot get out, due to the obstruction at the cervix by the placenta. (Fig. 6.)

Table II shows that in 712 patients the bleeding was "very slight" or "slight" and was therefore so small in quantity that it could not have had any influence in the separation of the placenta.

That the retroplacental hematoma is neither desirable nor necessary is evident from the fact that in the larger animals, such as the mare and the cow, the placenta is expelled without any hematoma formation; in fact without any loss of blood at all.

Placental separation is due to the fact that after the baby leaves the uterus, the uterus contracts and is reduced in size. The placenta cannot accommodate itself to this reduction in size, it is therefore cast off from the uterine wall. This mechanism alone is sufficient to cause the

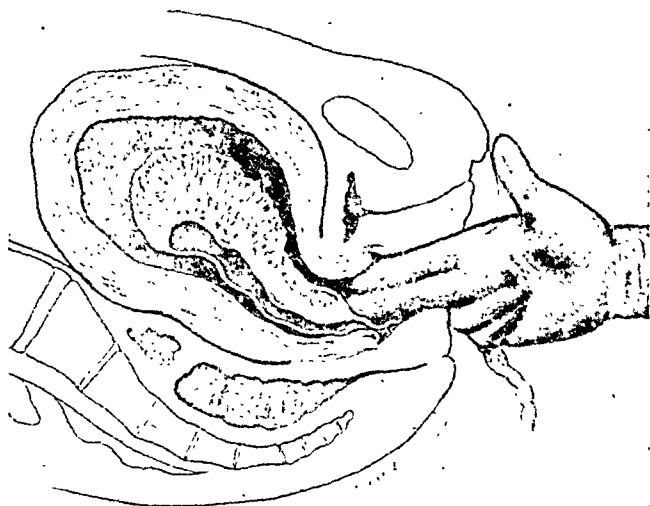


Fig. 1.—Vaginal examination to determine separation of the placenta. The placenta is separated, it lies loose in the uterus and cervix. Cervix is dilated. Placenta is ready to be expressed.

separation of the placenta. There is no need of the retroplacental hematoma to aid it in the separation, nor are there any other forces required to accomplish this.

The placenta cannot separate slowly, a small part at a time. For we know that when the placenta separates, bleeding occurs from the site of attachment, until the contractions and retractions control the hemorrhage. If the placenta separated a small part at a time, the uterus would have to contract correspondingly, in order to keep pace with the placenta, so that the contractions of the uterus would have to be in the form of a slow peristalsis. This does not happen. The uterus either contracts or relaxes as a whole and not in parts, so that the placenta comes away as a whole.

Furthermore, we know that "bleeding is from the placental site, which cannot retract until the placenta is completely detached"

(Polak). Therefore it takes about thirty minutes for the placenta to become separated and the uterus could not retract in the interval, the bleeding would have to continue, as there would be no way of controlling it until the placenta had completely separated. Fortunately the bleeding does not have to continue for any length of time, because the entire placenta separates promptly after the birth of the child.

Credé in 1861 claimed that the placenta separated in a few minutes and therefore he advised its early expression. Credé's opinion held sway until 1880, when Ahlfeld (supported by Dohrn) brought forth his view of noninterference or a "hands off" policy, and claimed that the expression of the placenta as advised by Credé caused more bleeding. He advised waiting for hours until the placenta came away by itself, in spite of the fact that in only 14 per cent of his cases did the placenta come out spontaneously. It is now conceded that such an attitude is

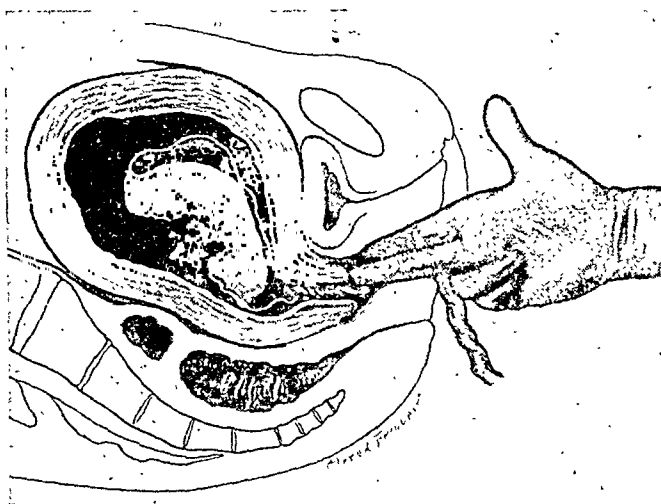


Fig. 2.—Vaginal examination shows cervix closed. Placenta cannot be delivered although it is separated.

both illogical and dangerous. Nevertheless it has had its influence in forming a sort of compromise between Credé's advice of early expression and Ahlfeld's policy of watchful waiting. But there is no more reason for waiting one-half hour before expressing the placenta than to wait several hours.

The reduction in the size of the uterus besides causing the separation of the placenta, forces it down into the lower uterine segment and cervix. The placenta can thereby easily be palpated by the examining fingers. In 80 to 90 per cent of the cases, the placenta is ready to be delivered without delay. But in 10 to 20 per cent of the cases when the uterus contracts, the cervix closes down and prevents the placenta from being expelled. (Fig. 2.) This closing down of the cervix prevents us from expressing the placenta routinely as soon as the baby is born. There is no way of knowing whether the cervix is open or

closed, except when vaginal examination is made. The cervix either closes down completely or partially, and it is then necessary to wait until it opens up again. It is useless to make any efforts at expressing the placenta until the cervix is sufficiently open to permit the placenta to pass through.

Another condition which occasionally causes some delay in expressing the placenta, occurs when part of the placenta is attached quite low, just above the cervix. The uterine contractions succeed in detaching the placenta; but that part of the membranes which is located just above the cervix remains attached. This fact can also be ascertained by the examining finger (Fig. 3), and the membranes can be detached while doing the examination. The placenta is then easily delivered.

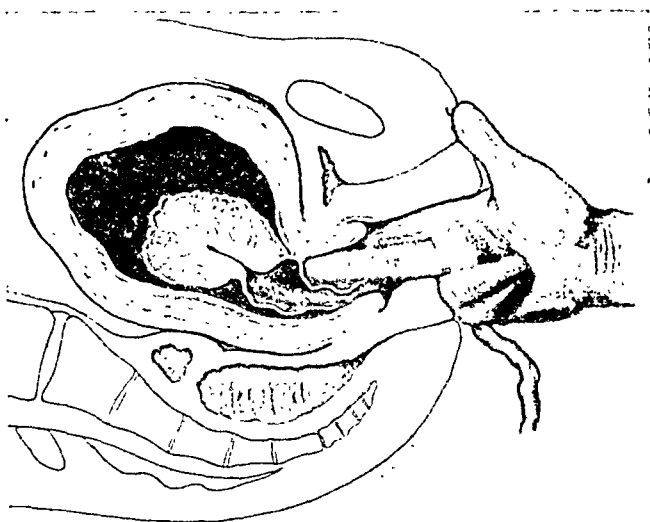


Fig. 3.—Vaginal examination discloses part of membrane attached, although the placenta and the rest of the membranes are separated.

The rare cases of pathologically adherent placenta are not considered in this discussion.

Before birth the placenta may be attached at any part of the uterus. When it separates and is forced down into the cervix it comes to lie in various positions. If situated on either side of the uterus, it naturally presents according to the method designated as the Duncan. Whereas if it had been centrally located, it will present itself according to the Schultze method. These two methods are only different forms of presentations, but there is no difference in the mechanism of separation in any case. Besides these two types in which the placenta presents after separation, it may present in a variety of forms, all depending upon its previous attachment. It is necessary to know where the placenta is located after separation in order to use the proper technic in expressing it.

Simple expression or the Credé maneuver will succeed in expressing a great many placentas but it will fail in quite a large number. Simple expression or Credé maneuver is quite applicable when the placenta presents according to the Schultze method. It is not applicable when the placenta lies either toward the right or left side of the uterus as in the Duncan method, or on the anterior or posterior wall. The Credé maneuver, in these cases, compresses the uterine cavity and interferes with the expulsion of the placenta. (Fig. 4.) For these presentations of the placenta, we must modify the technic so as to exert the pressure on that part of the uterus where we find the placenta located, and direct the force downward and toward the outlet (Fig. 5). When ex-

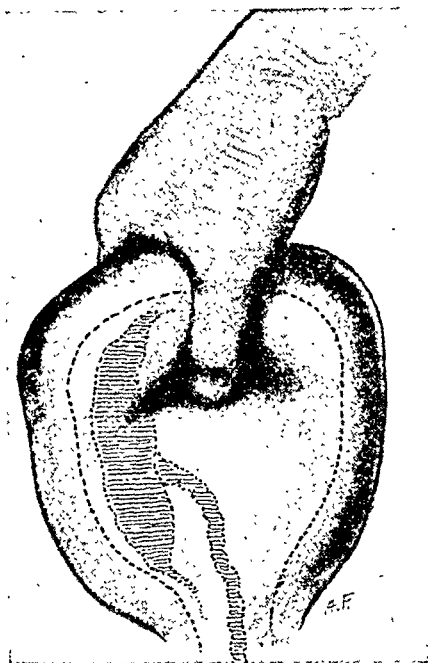


Fig. 4.—Ineffective Credé maneuver. The uterine cavity is compressed but as the placenta lies to one side, it cannot be expressed by this method.

pressing the placenta, the woman should be asked *not* to bear down but to relax; for if she attempts to bear down, the abdominal muscles become tense, and grasping the uterus is impossible. Full details how to express each individual placenta cannot be given. That knowledge is acquired when the vaginal examination is made and the placenta is felt. Depending upon where the placenta is found, the direction of the force is exerted accordingly.

One of the causes of failure in expressing the placenta is due to the uncertainty of whether the placenta has really separated. A half-hearted effort at expression is then made without success. However, by vaginal examination we know definitely whether the placenta is separated and when the cervix is open, we can attempt expression with full confidence that it is ready to be delivered.

The most important result of determining placental separation as soon as the baby is born and in delivering it promptly, is that it prevents unnecessary loss of blood. Table II shows the amount of blood lost in these 1000 cases. The "very slight," "slight" and "moderate," which total 95.5 per cent of the cases in this series, are all quantities that would be considered less than the normal blood loss in favorable cases.

The conservation of the patient's blood is the all important factor in the third stage of labor. Ahlfeld in conducting the third stage of labor by prolonged waiting had observed that a woman may lose 1500 c.c. of blood without any ill effects, though in other cases it proved fatal. He also showed cases that had lost 3000 c.c. of blood with com-

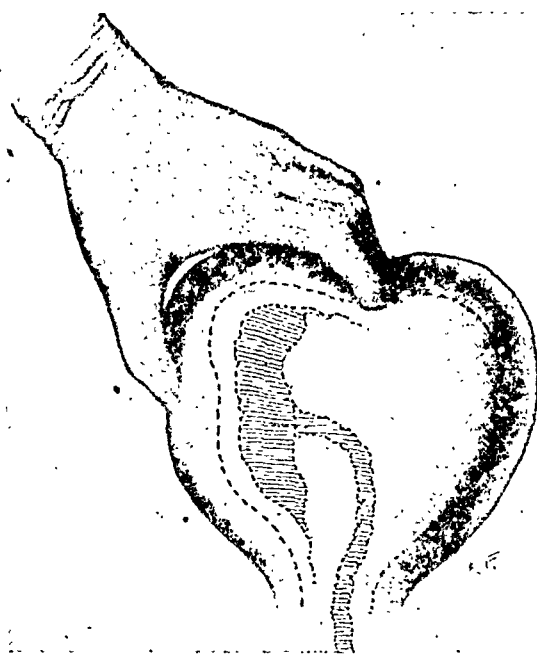


Fig. 5.—Technic of expressing placenta depending on its location. Pressure is made on that part of the uterus where the placenta is located.

paratively little disturbance. The fact that a woman in labor can tolerate an excessive loss of blood is no reason or excuse for permitting her to lose more blood than is absolutely necessary. We never know which patient will be unable to stand the loss. It is very fortunate that nature has provided a woman with the extra amount of blood so as to protect her in this dangerous period. In the evolution of the race those that were not so protected could not have survived. But that does not justify us in wasting the blood that she can use to good advantage during her postpartum period.

When the repair of the perineum is necessary, we should first deliver the placenta and make sure that the uterus is firmly contracted. Not only because the placenta in being delivered may tear the sutures, but

what is of greater importance is to prevent the uterus from filling up with blood while we are busy with the repair. If the repair is commenced before the placenta is expelled, it is essential that frequent attention be given to the separation of the placenta and to express it as soon as it is loose; for the time of separation of the placenta bears no relation to the time that it takes to repair the perineum. When the placenta is expelled and the uterus is well contracted, then we may safely proceed with any repair, without any uneasiness as to what may still happen when the placenta is delivered. While the first stage of labor may take days, and we need not interfere, and the second stage may be prolonged for hours and be of advantage to the patient, the minutes of the third stage are very precious and must not be wasted.

As the entire placenta separates at one time and the uterine bleeding comes from the placental site, therefore any bleeding coming from the

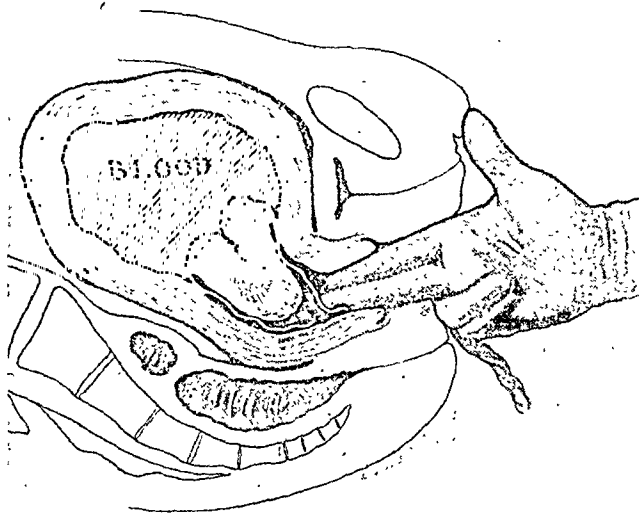


Fig. 6.—Vaginal examination shows placenta separated and presenting according to the Schultze method. The placenta obstructs the cervix, and blood accumulates in back of the placenta, without any external evidence of it.

uterus, irrespective of the quantity, may be taken as a sign that the placenta has separated. But the placenta may separate and not give any external evidences of bleeding (Fig. 6). In this series, 267 cases showed bleeding before the delivery of the placenta, while 733 gave no evidence of bleeding.

When thorough asepsis has been maintained during labor, there should be no hesitancy in doing vaginal examinations in the third stage. There are no ill effects from such examinations. The morbidity is reduced, and the patient recuperates sooner, because of the diminished loss of blood.

The procedure which I advocate for the third stage is as follows: As soon as the baby is born the nurse follows down the uterus with her hand. The baby is then cared for by tying the cord, treating the eyes and placing an identification tag on it.

A vaginal examination is then made (Fig. 1). With two fingers of the right hand in the vagina, the tips of the fingers feel the separated placenta lying loose in the cervix, or lower uterine segment. The cervix being open, the placenta is expressed with the left hand on the abdominal wall making pressure on the uterus in a manner indicated above. If desired the nurse can make this pressure on the uterus; and she continues to hold the uterus after the placenta is delivered.

If on examination the cervix is found to be closed (Fig. 2) nothing is done further until it relaxes. In that case examination has to be repeated to ascertain when the cervix opens up again, then the placenta is expressed in a similar manner.

One cubic centimeter of the pituitary extract is then given hypodermically, and two drams of ergot by mouth, and the third stage of labor is completed.

#### SUMMARY

1. The generally accepted signs of separation of the placenta are not dependable.

2. The only positive way of knowing when the placenta has separated and when it is time to express it, is by vaginal examination.

3. The placenta separates promptly after the birth of the child.

4. The retroplacental hematoma is not a factor in the separation of the placenta, but is the result of the placenta staying in the uterus after separation.

5. The cervix frequently closes down on the placenta. No attempt at expression should then be made until it opens up.

6. Besides the Schultze and Duncan mechanism, the placenta presents in various other positions, depending on where it had been situated when still attached.

7. Simple expression or Credé maneuver is not effective in a great number of cases. The technic of expression must depend on where the placenta is located after separation.

8. The repair of the perineum should be done after the placenta is delivered.

9. In the series of cases studied, the average time of the delivery of the placenta in 1000 cases was four and three-tenths minutes.

10. Because of the prompt expression of the placenta the uterus contracts sooner and firmer and bleeding is greatly diminished.

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15 EAST ONE HUNDRED ELEVENTH STREET.

## QUININE REACTION FOLLOWING RECTAL ANALGESIA

BY GERALD W. GUSTAFSON, M.D., INDIANAPOLIS, IND.

(From the Department of Obstetrics of Indiana University Medical School)

NOW that rectal analgesia is an established and worthy aid in obstetrics, it seems only fitting that we should note any possible contraindication or indication for modification which may present itself.

Dr. Losee of the hospital laboratory at New York Lying-in Hospital has obtained quinine from the urine, by qualitative analysis, in 92 out of 100 patients who had had rectal analgesia.<sup>1</sup> However, in 5,800 cases having had rectal analgesia at that institution no quinine reaction was observed aside from some cases having the minor symptoms of ringing in the ears and deafness.

For the past four years I have been using rectal analgesia and have never encountered a case of severe quinine reaction until the one reported below. Neither have I been able to find a case reported in the literature.

G. F., a secundipara, was admitted to the Methodist Hospital February 19, 1929, in labor. She was referred to me by her family physician, who had been in attendance, because of prolonged labor. She had had a normal delivery five and one-half years previously. During the present pregnancy prenatal care had been given by her physician, who stated that she had been entirely normal throughout. Her pains had begun at 2:00 A.M. on February 19, 1929. At 3:15 P.M. on that date she was admitted to the hospital. She had had no medication previous to admittance.

*Physical Examination.*—The patient was a rather large woman and very apprehensive. Temperature 99.2°, pulse 90, respiration 22. Heart and lungs were normal. Blood pressure 142-40. Urine showed a faint trace of albumin, but no casts. Abdominal examination showed the ovoid to be longitudinal and the pregnancy at term, the fundus reaching almost to the xiphoid process. Palpation revealed the head fixed in the pelvis, the breech in the fundus, back on the right and extremities about the midline. Fetal heart 144, regular, and heard in the outer portion of the lower right quadrant. There was no edema. Pelvic measurements were normal: 24, 27, 30, 19, 8. After an enema and catheterization, rectal examination showed membranes intact, dilatation 8 cm., engagement 2 cm. above the

<sup>1</sup>Harrar: AM. J. OBST. & GYNEC., 13: 486, 1927.



spines, position O.D.P. and no overriding of the head. Pains were of fair strength and coming at two- to three-minute intervals. Diagnosis: Pregnancy at term; position O.D.P.; no disproportion.

At 4:45 P.M. patient was given rectal analgesia, including 20 grains of quinine alkaloid. In a very few minutes she was much relieved and her contractions were not slowed. At 5:30 considerable bloody show was present and another rectal examination disclosed complete dilatation, membranes intact, position O.D.P. 135°, and the head at the level of the spines. Five minutes after the rectal examination the membranes ruptured spontaneously. The patient delivered spontaneously at 6:30 P.M. a 6 pound 14½ ounce boy in good condition. Third stage was entirely normal, lasting fifteen minutes.

The next morning the patient was entirely covered with a bright red erythematous rash and complained of intense itching all over her body. Her first question was whether or not she had been given any quinine, and she stated that the smallest dose of quinine caused her to have an identical rash with intense itching. Frequent soda baths and application of calamine lotion relieved her somewhat, but she insisted that the discomfort which she experienced for the following four or five days was worse than that of her labor. At the end of that time the rash gradually faded and the itching grew less. The babe's skin was always clear and both patients were discharged on March 5 in excellent condition.

#### COMMENT

Recently at the Wm. H. Coleman Hospital I delivered a colleague's wife, who gave a history of marked generalized edema, extensive skin rash and itching, following the administration of four grains of quinine sulphate by mouth. Having this history and the experience of the case reported, I gave the rectal analgesia omitting the quinine, with good results. According to Harrar<sup>1</sup> 30 cases were tried at New York Lying-in without quinine and some second stage delay was noted.

#### CONCLUSIONS

1. That quinine is absorbed when administered rectally in 20 gr. doses, is proved by clinical evidence.
2. A history of severe idiosyncrasy to quinine is a contraindication to rectal analgesia as generally employed.
3. In those rare cases of severe quinine idiosyncrasy, quinine should be omitted from the formula. Then rectal analgesia may be used with good results.

508 HUME MANSUR BUILDING.

# Society Transactions

## NEW YORK OBSTETRICAL SOCIETY

STATED MEETING, MAY 14, 1929

DR. W. J. DIECKMANN read a paper entitled **Further Observations on the Hepatic Lesion in Eclampsia**. (For original article, see page 757).

### DISCUSSION

DR. JAMES EWING (by invitation).—The pathogenesis of eclampsia is by no means a new topic. In fact, ever since Juergens described the original lesion, in 1867, without a satisfactory explanation of its origin, there have been numerous attempts in many centers to unravel the various stages by which this peculiar hemorrhagic hepatitis develops. Attention has been directed strongly to the probability of a placental, uterine, or intestinal origin of a poison, and that theory still maintains its popularity.

About twenty years ago the literature was quite full of experimental efforts to produce the lesion of eclampsia, and in nearly all instances the experimenters succeeded in producing lesions in the liver which bore some resemblance to eclampsia, and in not a few of those cases they laid claim to a complete success. Many agents have been employed for this purpose of intestinal, placental, fetal, or uterine muscle origin. It has been shown that several extracts, injected into animals will damage the liver and produce lesions which have many of the features of eclampsia. However, I think the authors are to be congratulated in having taken into account one very important new point which most of the previous experimenters have omitted. They have drawn to their aid the known fact that there is an increase in fibrin content of the blood and have made that, I judge, a rallying point to develop their experimental work, and by the injection of agents which reduce the clotting time of the blood they have succeeded in producing the hepatic lesions. I cannot say that these lesions, so beautifully shown are not observed in eclampsia, especially the hemorrhages in the periphery of the lobule; that seems to be a very suspicious lesion. In some forms of toxemia of gestation the lesion begins in the intermediate zone, but that is not the rule. In some instances in these experiments the hemorrhage began in the intermediate zone. That fact does not at all militate against their theory, because both those types are observed in the toxemia of pregnancy and in some cases of eclampsia.

They further support the theory by drawing upon the idea of placental cell emboli. Here I would like to have heard a little more detailed estimate of the extent to which those emboli actually occur. I conceive that as being, as a rule, a minor event in the course of gestation. It is true that in practically all lungs, after labor, by very careful sections, you can find small numbers of placental cells. I have seen them, but they are not very numerous, not anything like a flooding of the pulmonary capillaries by placental cells. I do not believe that occurs, so I would be much better satisfied with the strength of the supporting hypothesis which the authors use, if we had a little better estimate of the extent to which those emboli occur. Yet it may increase the coagulability of the blood.

They bring out the idea that tissue juices are liberated when the lining placental cells break loose and that further reduces the coagulation time of the blood. Whether such erosions of the placental villi can account for the reduced clotting time of the blood of gestation is open to question. That is a new idea

to me, and it will require a little while before I can fully digest it. While both those hypotheses no doubt support the theory, I question whether either of them is adequate to account for the change in the clotting time of the blood.

It is generally believed that the reduced clotting time of the blood is due to the increased amount of fibrin produced by the liver, which has a peculiar physiologic function in gestation and which necessarily has nothing to do with placental emboli or the discharge of tissue secretions into the blood. It is not so much that the blood clotting time is reduced in eclampsia by some agent which renders the fibrin factors more active, but that there is an actual increase in the amount of fibrinogen thrown into the blood by hyperfunction of the liver. Therefore there is a little difficulty in explaining theories and linking them with the hypertension of gestation, which is an essential factor of the condition.

As to the identity of these lesions with those of human cases, I believe that they are justified in assuming that many of these lesions are reproduced in eclampsia, but whether the essential element in the eclamptic lesion is so reproduced I am unconvinced.

Many years ago I was extremely interested in this question of eclampsia. I never was able to reach any conclusion as to the mechanism of those little hemorrhages in the eclamptic liver until a case came in from the Lying-In Hospital, which had died after a single convulsion with a large cerebral hemorrhage, the symptoms having lasted only a few hours. In that liver there were the most exquisite lesions of eclampsia in a very early stage, and when the sections were cut I was astonished to find a lesion I had never seen before. The entire fine hepatic arterial system was thrombosed, the vessels stood out like hyaline pipe stems, the lumina were occluded, the portal system was entirely free from distention, but here were these hepatic arterioles, not hepatic veins, or portal veins, but hepatic arterioles, which were the seat of this very grave lesion which clearly accounted for the miliary hemorrhages. On careful staining it appeared that this lesion began with hyaline necrosis of the endothelial cells of the hepatic arterioles, soon followed by fusion of the muscle coats of the arterioles until both were a solid hyaline mass. I do not believe any lesion produced in the portal system will produce such infarcts. Farr may never have seen that lesion. I cut many livers before I saw it. Since then I have seen traces of it in the older and more complicated cases.

The existence of such a lesion as the primary factor in the liver is inconsistent, one must admit, with the theory of a portal toxin that would strike the portal veins instead of the hepatic arterioles. Moreover, the same hyaline necrosis of the small arterioles occurs in other portions of the body, and sometimes quite notably. I have seen them in the gastric mucosa, in the pia mater, and in the brain, so we must assume that there is a general condition, as well as a local hepatic lesion of this sort occurring in the disease.

So I am unwilling to accept the author's belief as to the pathogenesis of the lesion of eclampsia. If one assumes that this is a correct explanation of the hemorrhages then I think it is going to be very difficult to establish a theory of portal intoxication.

It seems to me that the liver lesion is the most marked, because this disease is essentially a disturbance in the hepatic functions. It occurs in all phases of toxemia of pregnancy but takes this particular form only in eclampsia when convulsions are added. Any theory of eclampsia must have some bearing upon the other phases of toxemia of pregnancy. The only theory which meets these requirements is the theory of a primary disturbance in the function and circulation of the liver, which in pernicious vomiting and in acute yellow atrophy leads to degeneration of the liver cells, inhibition of the urea-forming functions of the liver, disturbance

of circulation, sometimes in pernicious vomiting to zonal necrosis, but which only in eclampsia gives rise to this peculiar thrombosis of the hepatic arterioles.

Now, having done my duty as a critic, measuring our colleagues and friends up to the highest possible standards, which I am sure they appreciate more than useless compliments, I want to say in conclusion that I feel they should be congratulated in planning a sane, rather subtle and reasonable line of experimentation in studying the pathogenesis of this extremely important disease. I believe that this may be a contribution of importance. I would not be at all surprised if they have pointed out an essential factor in the disease, and that by further pursuing this line of work they may be able to throw more light upon the undoubted connection between the pregnant uterus, the fetus, and the lesions in the liver. It is in that direction apparently that the best prophylaxis and therapy have been obtained.

DR. OTTO SCHWARTZ (by invitation).—Professor Ewing has called attention to the fact that he has observed thrombosis in the hepatic artery in cases of eclampsia. I was well aware of this fact and have studied the pictures of one of Professor Ewing's cases in Kosmak's monograph on "The Toxemias of Pregnancy." That this is a frequent finding is in my opinion very questionable. In the first place if this were true we might expect arterial thrombosis in other organs of the body. This only happens in very unusual cases of the very severe type. Also the hepatic artery even in smaller branches has a comparatively thick wall and a comparatively small lumen. It seems to me that on account of the character of the tributaries of the portal vein, that is, their thinner walls with larger lumina, thrombosis followed by rupture and hemorrhage in the periphery of the lobule is more apt to occur there than in the hepatic arteries. One cannot entirely put aside the fact that by good prenatal care in the last months of pregnancy, chiefly the elimination of meat protein from the diet and good elimination of bowels, eclampsia seldom develops. In other words, the absorption of substances derived from meat protein are in greater concentration in the portal system than elsewhere and under the condition of pregnancy, if this concentration becomes marked, it may cause coagulation with subsequent hemorrhage and necrosis of the liver.

DR. DIECKMANN (closing).—Dr. Ewing spoke of the difficulty of finding chorionic villi in the lungs and the hyperinosemia which occurs in eclampsia. We believe that the increased fibrinogen in pregnancy is due at least in part to the stimulation produced by the setting free of tissue fibrinogen. The latter substance is extracellular and a small amount is freed whenever there is a breaking off of a villus. *In vitro* Mills has proved that the fibrin yield from a given plasma may be made to vary greatly by tissue extract addition, variations being noted up to 152 per cent above normal. Fibrinogen by mouth in doses of 3 c.c. (maximum concentration 1.5 per cent) on an empty stomach will within five minutes reduce the clotting time of the blood in the finger tip, 20 to 60 per cent. In many cases of eclampsia the coagulation time is very short, thus indicating why it is difficult in many cases to bleed them.

We believe that other factors are also concerned in eclampsia. For example, some substance or substances must be causing the capillary spasm and hypertension. These products may have their source in the placenta, in the intestinal tract or in a damaged liver.

A report by Copher and Dick of the "stream line" phenomena in the portal vein is of great interest to us. They show that there are three distinct and separate currents in the portal vein. Blood from the stomach, duodenum, and jejunum goes to the right lobe. In one case of human eclampsia we found that the lesion was limited almost entirely to the right lobe and in the experimental produc-

tion of the lesion by the oral route, whether we use tissue fibrinogen or meat, we find the most marked lesions in the right lobe, thus additional proof is furnished in support of the intestinal absorption theory.

We have also found that if we use a pressor substance such as tyramine, in conjunction with meat by mouth and fibrinogen intravenously, the lesion is more easily and quickly produced and is as a rule more extensive.

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## OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF MARCH 7, 1929

### DR. WILLIAM R. NICHOLSON reported a **Case of Simulated Uterine Rupture in an Aged Patient.**

This patient gave her age as seventy-three. Her relatives thought she was underestimating it somewhat. She was sent in to my service by Dr. Pfahler for diagnostic curettage, with the idea of a possible malignancy, as she had had slight vaginal bleeding recently. On examination an apparently senile uterus was found, with a tumor arising from the neighborhood of the right cornu. This tumor was about the size of an orange. Under the ribs on the right side there was another easily demonstrable tumor. No connection could be shown between this second tumor and the uterine growth. An anesthetic was given and the sound showed the cavity apparently about  $1\frac{1}{2}$  inches deep. The dilator was introduced to this depth, followed by a curette. Dilatation not being quite sufficient, the dilators were again introduced, when to my surprise they slipped in up to the shoulder of the instrument instead of  $1\frac{1}{2}$  inches. There was quite a little bleeding from the vagina within a few moments, and therefore upon the basis that there had probably been a perforation of the senile uterus, the abdomen was opened. There was no blood in the peritoneal cavity and investigation revealed no perforation. It was then clear what had happened. The uterus was not a small senile uterus, but was four inches in depth and in the fundus was a myoma which had grown up, elongating the tubes. From the top of this fundal tumor a pedicle ran to the other fibroid which was adherent under the ribs. This second tumor, adherent under the ribs, had angulated the uterus so that the whole body was pulled to the right, making a sharp angle of flexion. This angle had been straightened by the second introduction of the dilators. An hysterectomy was done, the tumor under the ribs being separated with some difficulty. The ovaries, which were adherent, were allowed to remain. On opening the uterus subsequently, it was found that there was a polyp just below the internal os, and that this was the cause of the vaginal bleeding. Fortunately, the patient recovered without symptoms.

### DR. LEWIS C. SCHEFFEY reported an instance of **Carcinoma of the Cervix in a Woman Twenty-Two Years of Age.**

Mrs. A. H., aged twenty-two, was admitted to the Gynecological Service, Jefferson Hospital, on July 4, 1928, complaining of continuous, foul, bloody discharge, accompanied by the passage of tissue-like material from the vagina.

Four months prior to admission she had been delivered spontaneously of her third child, previous pregnancies and labors having occurred in 1925 and 1926. During this recent pregnancy, she frequently had pains in the side, together with periods of bleeding each month. Following delivery, she never ceased to have a

bloody discharge, and in June her family physician decided to perform a curettage, following a profuse hemorrhage. At this time he recognized a proliferative growth in the vaginal vault, and was quite emphatic in stating that he had observed nothing abnormal about the cervix and vagina at the time of delivery. He proceeded no further and referred the patient to the hospital for further study and treatment.

The past history was uneventful, although the patient reported a leucorrheal discharge since the first labor in 1925. There had, however, been no abnormality of menstruation or irregular bleeding prior to the onset of the recent pregnancy.

The patient presented a toxic, somewhat emaciated appearance, and examination showed the cervix to be obliterated and replaced by a friable, bleeding, cauliflower-like growth, club-shaped, extending two-thirds of the distance to the vaginal orifice, and markedly distending the vagina. It was partially fixed and appreciably tender, clinically a Class III carcinoma. The fundus was palpable and movable, the adnexa not being distinguishable. A portion of tissue was readily removed for histologic study, Dr. C. J. Bucher reporting squamous cell carcinoma. The Wassermann was negative, the blood count showing a pronounced secondary anemia and leucocytosis (Hgb. 47; R. B. C. 2,480,000; W. B. C. 14,000; C. I. P. 97). The urine was negative. Intermittent fever was present, and the sedimentation test vertical in type, complete settling occurring in thirty-five minutes.

A few days later (July 9, 1928), under nitrous oxide and oxygen anesthesia, I excised this large carcinomatous mass and cauterized the base, 125 mg. of radium being implanted into the remnant of the cervical canal and around the periphery of the growth for thirty-six hours. Very little reaction was observed and the patient left the hospital in ten days.

I have seen this patient upon two occasions since then, her most recent visit to the Clinic occurring during the past month. Locally the cervical area shows the usual postradium appearance, all slough having disappeared. Moderate pericervical induration is present, the fundus being normal in size and freely movable. Vaginal discharge is negligible, and no bleeding has occurred since the radium application. A striking feature has been the marked gain in weight, in part attributable to the effect of the radium dosage on the ovaries, I presume. Her general condition appeared to be splendid. The future aspect of the patient is problematical of course, and we are observing her with more than usual interest.

#### DISCUSSION

DR. C. C. NORRIS.—In a series of over 4,000 cases recently reviewed there was not one under twenty years of age, nor have I ever seen so young a patient.

A point of interest in Dr. Scheffey's case is that it was first observed during the puerperal period. At this time and during pregnancy extensive erosions often exhibit some of the characteristics of malignancy. Biopsy is a valuable aid in the diagnosis of all really early carcinomas, and especially so in this type of case. In Dr. Scheffey's case there is no question of the correctness of the diagnosis, and it seems to be either a transitional or squamous cell type.

As to Dr. Nicholson's inquiry regarding the dosage of radium irradiation for these cases, it varies in the hands of different operators. About 2,400 mg. hours is the minimum, and in some clinics much higher dosages are employed. In Stages I, II, and III, I usually employ not less than 2,400, or more than 3,200 mg. hours at the first treatment, and generally give such cases a second, and in some instances, a third irradiation. I govern the dosage after the initial treatment by the conditions surrounding the individual case.

DR. JOHN C. HIRST presented an **Analysis of Eighty-Four Consecutive Cesarean Sections.** (For original article, see page 773.)

### DISCUSSION

DR. F. E. KELLER.—In comparing one's own statistics with those offered, there are many points that should be considered. The manner in which I have done certain things differs diametrically from that stressed by Dr. Hirst, such as the preliminary dosage of morphine and the use of local anesthesia. Under these conditions we have done the vast majority of our operations. Also, we have not considered the disadvantage of preliminary vaginal examination; of course, the majority of our cases are in our own care preceding operation which has a good deal to do with it.

We are interested in the question of mortality and the hours of labor before cesarean section was performed. I appreciate the fact that many of these cases come from sources where it is impossible to regulate the hours of labor before section is performed, but it does seem that if these cases could have been seen earlier, the probability is that his mortality would have been greatly reduced. From some points of view, there are too many cesarean sections done, but when I personally consider some of the cases in which the vaginal delivery has been difficult, and where a vaginal operation has been necessary for delivery, with consequent mutilation of the child and mother, I feel that in some of them it would have been better for the mother and far better for the child if cesarean section had been done.

DR. P. F. WILLIAMS.—I would like to ask about the table showing the mortality in the emergency group of cases, as to the mortality comparison between the Beck and the classical operation.

DR. LONGAKER.—In view of what has been said, the matter of diagnosis of impending rupture and actual rupture following a prior cesarean section has great importance. I have seen three ruptures following cesarean sections and if this point is remembered, the diagnosis of impending and actual ruptures is easy, i.e., exquisite tenderness on gentle palpitation. \*

In our experience and that of my associate, Dr. Harriman, the greatest amount of satisfaction in our operative work has been derived by following the suggestions of Dr. Pitkin's paper read here a few months ago. The operative and postoperative results and especially the comparative bloodlessness of the operation have been in striking contrast with anything we have ever experienced before in a long number of years and amounting to over 125 cases.

One point I think deserves emphasis: I believe we fall down more frequently in the proper treatment of cases of cervical dystocia than anything else. These are the cases, often long drawn out with unfavorable results to the baby and, when ultimately operated upon, with bad operative results. What we seem to need is a clear definition of the indications for operative delivery in cervical dystocia.

DR. WM. R. NICHOLSON.—I would like to go on record as stating that there was no marked sensitiveness in my cases of secondary rupture following cesarean section, and that the diagnosis was far from easy. This is in direct contradiction of the statement made by Dr. Longaker.

DR. SCHUMANN.—I do not condemn spinal anesthesia. I am in favor of any anesthesia other than inhalation; if any physician wishes to go to the extra trouble of subjecting his patient to spinal anesthesia, that is his own concern. We have found cocaine perfectly efficient.

I do not agree with Dr. Longaker on the matter of his ability to diagnose imminent rupture by the exquisite tenderness. I have seen three such cases and in all three the woman was symptomless and a careful palpation of the abdomen in order to determine the position elicited no pain and yet the uterus was widely ruptured without labor.

DR. CHAS. S. BARNES.—I would like to add that in our case the almost symptomless condition was similar to that in Dr. Nicholson's; the symptoms were very slight and it was only because the pulse had increased in rapidity that we operated.

DR. BERNARD MANN.—Several years ago at the suggestion of Dr. B. C. Hirst, I began the suturing with the endometrium and a subperitoneal suture followed by a running Lambert suture of the peritoneal covering of the uterus, and there was much less distention of the abdomen and most of the cesarean sections were almost afebrile. I have recently used this method of suturing in a case of eclampsia with very good results.

DR. HIRST (closing).—Dr. Piper is modest about his special suture which is a decided advantage over the method which had been in use in the University Maternity up until four or five years ago. There is undoubtedly less fever and less distention following it, and it leaves the uterus low instead of up around the umbilicus, as sometimes occurs after careless suturing of the uterus. I agree with Dr. Keller's remarks about the advantages of morphine with local anesthesia. However, morphine given with nitrous oxide or ether, has a bad effect on the baby. As to the length of labor, we allow no patient to have a longer test than twelve to fourteen hours with the first baby and two or three hours shorter test after the first child, but of course many patients in this group were admitted with the history of much longer labor prior to admission.

I am unable to answer Dr. Williams' question as to the division of mortality according to the Beck operation or the other types of procedure.

Answering Dr. Nicholson's questions as to whether we believe in the dictum: "Once a cesarean, always a cesarean," I would say that cases operated upon for dystocia invariably should have a section with the next child. If cesareanized for premature separation, placenta previa, etc., then, other things being equal, it is not dangerous to allow a short test of labor for the next child, provided the patient be in a hospital.

DR. E. A. SCHUMANN read a paper entitled **Further Observations Upon Hydatidiform Mole.** (For original article; see page 768.)

#### DISCUSSION

DR. WM. R. NICHOLSON.—I recently saw a case in which curettement in a supposed incomplete abortion showed the presence of a hydatid mole. At the first operation the hemorrhage was so profuse that the assistant who performed it packed the uterus. A week later the woman still bled freely enough to warrant a second packing. The subsequent history of this case was a gradual increase in anemia, with slight spotting. Two blood transfusions were given and the ovaries exposed twice to x-rays. Finally, consent to radical operation was obtained. Upon opening the abdomen it was found that we were dealing with a marked bicornuate uterus, the one horn being as large as a large adult first, the second being practically normal size for an unimpregnated uterus. Dense adhesions between the uterus and sigmoid were present. Supravaginal hysterectomy was performed. The pathologist reported the presence of synecioma in the fundus of the pregnant uterus and two perforations in the wall, which he believed to be due to the malignant process



present. The woman died of apparent peritonitis. No postmortem was permitted. It is to be remembered that this condition is comparable, in so far as vigorous curettage is concerned, with placenta accreta, and therefore that rupture of the uterus is very possible.

DR. CLIFFORD B. LULL.—I would like to report a case which I thought was one of abortion but which proved to be a large hydatiform mole. Under anesthesia I examined the interior of the uterus and could find no trace of mole. I believe, too, that if you have a patient with hydatiform mole, the most logical thing is to open the uterus as there is always the possibility of malignancy. Our patient made a good recovery, and we informed her of the possibilities of further difficulties. She had one normal menstrual period after discharge from the hospital and two weeks later had continual flow of blood from the uterus. On examination the uterus was unquestionably larger than it should be, and we were uncertain as to whether subinvolution or malignancy was the cause. I advised hysterectomy or if not that, to allow an exploratory. She refused to have anything done.

DR. C. C. NORRIS.—My experience in the histologic diagnosis of curettings is in general similar to that of Dr. Schumann.

The histologic diagnosis of chorionepithelioma is in many cases impossible, except in the type referred to by Ewing as choriocarcinoma. In this connection I believe that many uteri have been sacrificed due to an incorrect diagnosis. When the pathologist is in doubt he should so report to the surgeon. In the case of doubt the surgeon is in a better position to make a decision than is the pathologist. I do not think the fact that even the experienced pathologist is not always able to arrive at a positive histologic diagnosis in these cases is generally recognized.

DR. SCHUMANN (closing).—I would simply like to emphasize the statement that diagnosis of potential malignancy is impossible from microscopic examination. The reason I so strongly advocate hysterotomy is that the primary mortality from hemorrhage and sepsis is less. It is true that in skilled hands it is possible to manually remove a mole without mortality in a number of cases, but then four or five patients will come along who are poor surgical risks and a high mortality rate follows, which could have been avoided by employing abdominal hysterotomy.

Furthermore, I am coming to believe that chorionepithelioma is a rare disease. Recently Dr. Macfarland, who is now making a survey of all cases in the Pathological Department said he had yet failed to find more than one case of chorionepithelioma. At the Jefferson Hospital I noted but two or three and Dr. Bland reported one recently. Symmers, reporting over a period of eighteen years at the Bellevue Hospital, says: "This disease, which we all regard as rather common, is exceedingly rare."

# Department of Reviews and Abstracts

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CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

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## Selected Abstracts

### Pregnancy and Disease

Hofbauer, J.: Contributions to the Etiology of Pyelitis in Pregnancy. Bull. Johns Hopkins Hosp. 42: 118, 1928.

The author summarizes his study as follows: Urinary obstruction in pregnant women is caused by certain anatomic conditions in the juxtavesical portion of the ureter and in the trigonum vesicae.

Hypertrophic changes in the musculature associated with hyperplastic changes in the connective tissue are essential factors in the narrowing of the lumen of the lower part of the pelvic portion of the ureter. The constriction is still further accentuated by an encircling ring resulting from hypertrophy of the ureteral sheath, while engorgement of the vessels in the mucosa and dextrorotation of the uterus may act as contributory factors.

There was no demonstrable indication of an active inflammatory process or of remnants of a preceding inflammation in the ureteral wall in the specimens examined.

A moderate degree of hydroureter is a common occurrence in pregnant women. The distal end of the ureteral dilatation usually lies at the level of the parametrium, the visible dilatation being associated with a demonstrable delay in ureteric action. The hyperplastic and hypertrophic changes in the upper pelvic portion and in the abdominal portion of the ureter are decidedly less marked, and the dilatation above the narrowed area of the juxtavesical portion occurs as a consequence of the structural peculiarities described in the article.

The hypertrophy of the trigonum accounts for the clinical phenomenon of residual urine in pregnant women.

In seven out of 55 cases a definite lowering of the opsonic index of the serum toward *B. coli* during pregnancy could be demonstrated. The bearing of these findings on the development of actual pyelitis is discussed.

While there occurs after labor a gradual return of the renal pelvis and of the ureter toward normal in uncomplicated cases, persistence both of bacteria and of marked dilatation of the ureter was demonstrable on reexamination in a considerable percentage of women who had been treated for pyelitis during a preceding pregnancy. In the majority of these cases, the level above which the ureter has remained dilated corresponds to the parametrium. Stricture of the ureter may occasionally result from long-standing infection in the ureteral wall during pregnancy.

The inadequacy of the present therapeutic measures calls for radical changes in the treatment of pyelitis complicating pregnancy. The use of pituitary extract is suggested on account of its specific antiphlogistic action, as well as for its stimulating effect upon ureteric peristalsis.

C. O. MALAND.

Frigyasi, J.: *Pregnancy and Gallstone Disease*. Med. Klin. 23: 1844 and 1926, 1927.

Pregnancy plays an important rôle in the formation of gallstones. In Mayo's 3075 cases of gallstones in women, 90 per cent had borne children and in 90 per cent of them the first symptoms of their trouble began during pregnancy or immediately afterward. The first condition necessary for the production of gallstones is stasis of bile, which is usually due to mechanical influences. Pressure by the uterus is not a factor but infection is considered by some writers to be an important cause. Westphal believes the cause of the stasis of bile is neither mechanical nor inflammatory but is a motility neurosis of the bile tracts which arises from an increased tonus of the vagus. Cholesteremia is considered to be an important factor in the production of gallstones but this point is not settled. It is true, however, that the cholesterin content of the blood serum increases during pregnancy and decreases during the puerperium.

The treatment of gallstones during pregnancy is the same as that in the non-pregnant state. The therapy should be conservative and an attempt should be made to influence the irritability of the vagus system and for this purpose anti-spasmodics such as atropine should be used. Scopolamine and morphine also give relief from the pain. To avoid stasis, exercise is prescribed and the diet is regulated. Heat applied locally, olive oil, pituitrin and magnesium sulphate may help. Medical treatment usually suffices, for in the author's series of 30 cases, operation was necessary only twice. In this series 63 per cent were multiparas.

J. P. GREENHILL.

Mann, F. C., and Higgins, G. M.: *Effect of Pregnancy on the Emptying of the Gall Bladder*. Arch. Surg. 15: 552, 1927.

About two years ago Boyden made the important observation that a meal of egg yolk and cream caused the gall bladder of a cat to empty. This observation has been the basis of much recent, very important work on the physiology of the biliary tract. Mann and Higgins studied dogs in various stages of pregnancy. Similar studies were made on gophers and guinea pigs. Control studies were made on nonpregnant animals.

Mann and Higgins summarize their experiments as follows: Their observations show that the gall bladder of the pregnant dog, guinea pig, and gopher usually does not entirely empty following a feeding of egg yolk and cream, while in the nonpregnant animal it usually partially or completely empties. Partial emptying was noted in early stages of pregnancy, and in a few dogs it was noted late in pregnancy. However, in no instance in the large number of animals observed did the gall bladder of a pregnant animal of these three species empty in the time and to the degree that it emptied in the nonpregnant animal. The gall bladder of one pregnant cat emptied in the same manner as that of a nonpregnant cat. A large number of pregnant cats and pregnant animals of other species must be examined before it can be accepted as a general physiologic fact that the gall bladder of the pregnant animal does not empty in a similar manner following the ingestion of the standard fat meal as it does in the nonpregnant animal. However, sufficient data have been secured in regard to three species to make it appear probable that similar observations will be made with other species, including man.

The results of these experiments cannot be applied to the human being without qualification. However, three considerations are pertinent to the subject. The pathologic conditions often associated with pregnancy which may directly or indirectly have some relation to the mechanism of the biliary tract are: (1) hyperemesis, (2) eclampsia, and (3) gallstones. Further observations with particular reference to the normal mechanism of the biliary tract must be made before definite conclusions can be reached.

D'Amato, G., and Gmelin, E.: *The Effect of Pregnancy and Puerperium Upon the Galltract.* Zentralbl. f. Gynäk. 51: 1031, 1928.

A large number of healthy pregnant and early puerperal women were examined with the duodenal tube. The obtained duodenal contents were examined chemically, bacteriologically and microscopically and were found not to differ at all from specimens gained from nonpregnant women. Cholecystography was also done in a number of healthy pregnancies. All gall bladders were visible, a considerable displacement to the right could be observed in the last months of pregnancy. Five puerperae with complaints suggestive of gall bladder involvement were examined, in two the shadow was very faint, in the three others no trace of a shadow was visible, considered to be due to a spastic condition of the ducts or a swelling of their mucosa. Gallstones were not seen in any of the cases. The investigators feel that cholecystography can be employed with success during pregnancy. In healthy pregnant and puerperal women the findings resemble those of the nonpregnant.

GROVER LIESE.

Brindeau, A., and Juge, C.: *Surgical Interventions During Pregnancy.* Gynéc. et Obst. 14: 10, 1926.

The legitimacy of surgical intervention during pregnancy is no longer questioned. It is admitted by all that the dangers formerly anticipated do not exist. In 113 women operated upon during pregnancy at the Tarnier clinic, 110 cures, were obtained with a mortality of 2.55 per cent. Of the operated women, 45 went to term without complications, 53 continued their pregnancy with no further data on their delivery, and 13 had interruption of the pregnancy following operations. The operations were done for the following conditions; ovarian cyst, 45; fibroma, 18; appendicitis, 18; salpingitis, 11; various operations, 21. In general, an operation is not more difficult in the pregnant woman, though there is more vascularity in the region of the genitalia. In 2 cases there occurred phlegmasia alba dolens. The anesthesia of choice should be chloroform or ether. Spinal anesthesia is contraindicated because of the danger of exciting contractions. Morphine should be given after operation every six hours. A definitely indicated operation should never be omitted because of the pregnancy.

GOODRICH S. SCHAUFFLER.

Fairbairn, John S.: *Acute Abdominal Emergencies Complicating Pregnancy and the Puerperium.* British M. J. 1: 456, 1927.

The author attempts to point out the difficulties that are encountered in diagnosing acute abdominal conditions that arise during pregnancy and the puerperium. The chief symptoms are vomiting, abdominal distention, jaundice, and abdominal pain.

When the vomitus is of a coffee ground type, progressing toward fecal type, associated with distention of the abdomen, and occurring after the fifth month without toxic signs the cause may well be other than pregnancy.

When jaundice is present, gall bladder disease must be differentiated from toxemia with liver damage. Toxemia with hepatitis is usually accompanied by abuminuria and severe vomiting. Epigastric pain is present in both.

Abdominal pain is associated with many conditions, the most important of which are intrauterine pregnancy with retained hemorrhage, spontaneous rupture of pregnant uterus, tubal pregnancy with rupture or leakage of blood, strangulation of ovarian cyst by torsion of pedicle, peritonitis (unusual from an infected tube), appendicitis, pyelitis or pyelonephritis of pregnancy.

Abdominal distention is usually from ileus and more frequently in patients who have had previous abdominal surgery with resultant adhesions causing strangulation.

Appendicitis late in pregnancy is found to be more dangerous because of the

high position of the appendix. Late diagnosis is frequent, as the pain is mistaken for labor. In appendicitis fetal movements are painful and there is unusually low temperature and disproportionately high pulse. The treatment is the same as in nonpregnant cases, except that expectant treatment is to be considered less strongly than in nonpregnant. The prognosis is graver because of the danger of abortion or premature labor after operation.

ADAIR-GRIMES.

**Jerlov, E.: Appendicitis During Pregnancy and the Puerperium.** *Acta obst. et gynec. Scandinav.* 4: Supplement, 1925.

The author studied in 21 hospitals and in the private practice of three physicians the case histories of patients who had appendicitis during pregnancy or the puerperium. There were altogether 456 such cases, of which 390 occurred during pregnancy and 66 during the puerperium. Most of the former cases appeared during the early months of pregnancy and two-thirds of the patients were under thirty years of age. Appendicitis in the puerperium was purely accidental. Since appendicitis occurred in only 1.3 per cent of all pregnant women, it must be concluded that pregnancy does not tend to increase the susceptibility to appendicitis. Appendicitis is definitely more frequent among nonpregnant women.

In mild cases of appendicitis, during pregnancy and the puerperium, tenderness is localized at McBurney's point, but in severe cases the tenderness extends through the lower right quadrant. The temperature is often low. It is important to rule out pyelitis, but often cystopyelitis occurs with appendicitis during pregnancy. Other pathologic conditions to be considered are acute salpingo-oophoritis, extra-uterine pregnancy, twisted ovarian cyst, cholecystitis, and cholelithiasis.

Pregnancy does not tend to cause a recurrence of an old appendicitis. In cases of appendicitis with peritonitis pregnancy has a bad influence. Labor does not affect mild cases but aggravates the cases complicated by purulent peritonitis when it precedes operation. When, on the other hand, operation precedes labor, the results are definitely better. In the mild cases of appendicitis, operated on during pregnancy, abortions occurred in only 13 per cent. In the severe cases the incidence of abortion was between 70 and 80 per cent. This was due to the purulent peritonitis which was present. In 19.2 per cent of the latter cases salpingo-oophoritis occurred.

The total maternal mortality among 263 cases was 9.5 per cent. Among the 167 mild cases there was no death but among the 96 severe cases the mortality was 26 per cent; hence the mortality of the mild cases in pregnancy is no greater than in nonpregnant individuals. In the case of an abscess, however, the mortality is higher in the pregnant than in the nonpregnant individual. The cases of diffuse peritonitis in pregnant women, on the other hand, do not have a worse prognosis than in the nonpregnant. The cases where abortion occurred had a high mortality, hence abortion is a bad prognostic sign. By the same token there is no indication to open the uterus before performing an appendectomy during pregnancy. There is no indication to perform a hysterectomy in the cases complicated by peritonitis. In all mild cases immediate operation should be performed but the uterus should not be evacuated. If the uterus is emptied before operation, the prognosis is much worse than if the uterus is emptied after operation. The uterus should not be emptied routinely after delivery. The best results will be obtained by waiting for a spontaneous delivery.

J. P. GREENHILL.

**Wilson, Robert A.: Acute Appendicitis Complicating Pregnancy, Labor and the Puerperium.** *Surg. Gynec. Obst.* 45: 620, 1927.

It is known that about 2 per cent of women with acute appendicitis are pregnant. About 80 per cent of the cases occur in the first six months, the disease being com-

paratively rare in the last trimester. It undoubtedly is more common in the puerperium than is generally supposed, but is frequently overlooked at this time. Pregnancy reacts unfavorably on a diseased appendix. It always aggravates the existing pathology and is likely to precipitate an acute attack at any time. Primary attacks during pregnancy are quite rare. The disease runs a rapid course, and perforation and peritonitis may be present in a few hours. This is especially true in the late months of pregnancy. The diagnosis becomes increasingly difficult after the sixth month, this being especially true if uterine contractions are present. The leucocyte count does not furnish much aid because of the leucocytosis normally existing during pregnancy. In case of doubt, operation should be performed. The maternal prognosis is good if an early operation is performed, but following perforation a mortality rate of 50 per cent is to be expected. In simple cases there is little danger of abortion, but if perforation is present, the uterus will empty itself in at least 50 per cent of the cases. The more advanced the pregnancy the greater is the danger to mother and child. Whenever possible, the appendix should be removed during laparotomies performed for other conditions. When the organ is known to be diseased, it should be removed before pregnancy occurs, and, if a pregnancy is already present, at the first appearance of symptoms. It is in the last trimester that several important problems have to be dealt with, and in order to meet these, cesarean section, followed by appendectomy, is advocated as the procedure which will give the best results. The method to employ in emptying the uterus depends on the extent to which the uterine wall is involved in the infectious process. When this is slight, the classical operation is indicated, but, if severe, a choice must be made between a low section or the Porro operation.

WILLIAM C. HENSKE.

**Portes and Seguy:** The Influence of Pregnancy, Labor, and Puerperium on Acute Appendicitis. Therapeutic Results. *Gynéc. et Obst.* 15: 114, 1927.

Pregnancy does not particularly predispose to appendicitis but appears to play an important rôle in the determination of exacerbations of previous chronic appendicitis. There seems to be a marked tendency to development of diffuse peritonitis of a serious nature, especially during labor, when the uterine contractions traumatize the cecoappendicular region, breaking protective adhesions and freeing infective elements. Nine previously unpublished cases are reported.

In view of the frequent exacerbations caused by gestation it is wise to operate before marriage upon every woman who has previously shown definite symptoms of appendicitis. In general, the mode of action should be approximately that which would be used if the pregnancy were not present. Intervention during appendicitis complicated by plastic peritonitis or abscess, definitely endangers the pregnancy (40 per cent of 38 patients miscarried). Under these conditions it is better to wait if possible; or if interference is necessary, to simply drain for the time being. In diffuse peritonitis, the only chance to save the mother is by immediate intervention. Hysterectomy has been suggested in order to facilitate drainage but this seems extremely radical. If operation is indicated during labor it should be performed.

GOODRICH C. SCHAUFLIER.

**Pewsner:** Appendicitis and Pregnancy. *Russian Clinics*, p. 559, 1926.

Pregnancy is an important factor in the aggravation if not primary origin of appendicitis. During pregnancy the process often is difficult of recognition, the symptoms mild, while in the puerperium the disease more quickly reveals itself in its true form. Appendicitis may interfere with the normal progress of pregnancy and cause its premature interruption, and is likely to complicate labor and especially the puerperium. If one acknowledges that every diagnosed appendicitis justifies operation, one will have to admit that in pregnancy even only suspicion of such a

condition indicates surgical interference. The dangers are so definite, that earlier in pregnancy, if the patient should definitely refuse appendectomy, the interruption of pregnancy must be considered justified.

AUTHOR'S ABSTRACT.

Heyer, E.: Inflammation of the Adnexa During Pregnancy. *Monatschr. f. Geburtsh. u. Gynäk.* 76: 243, 1927.

There are in literature, reports of 35 cases of purulent inflammation of the adnexa complicating pregnancy. In cases where these two conditions occur, the infection (1) may have occurred before conception, (2) it may have taken place during conception, or, (3) after conception. As regards the first possibility, in unilateral acute cases, pregnancy is possible. In cases of previous bilateral chronic inflammation, impregnation is possible because the tubes possess an extraordinary power of restitution. In fact, in chronic cases, pregnancy is the ideal method of cure because stasis and hyperemia are the chief aims in treatment of chronic inflammation. There is no proof that old chronic cases are lighted up by pregnancy. A case which has not completely run its course may be made worse by pregnancy.

Infection during conception is not uncommon where gonorrhea is present. The occurrence of infection after conception is doubted by most authors. Hence the coincidence of adnexal inflammation and pregnancy occurs chiefly in cases where there has been a unilateral subacute infection before conception. Of the 35 cases reported in the literature there were careful notes in 24 instances, and in 18 the infection was one-sided. The author reports an additional case.

The diagnosis is often difficult. As long as there is no pus present, conservative treatment is instituted just as in nonpregnant individuals. Where pus appears, surgical interference is indicated without delay and especially by laparotomy. Among the reported cases there was a mortality of 30.4 per cent for the patients who were operated upon and a mortality of 100 per cent for those not operated. All the patients who were operated upon before perforation of an abscess, recovered.

J. P. GREENHILL.

Placintianu, G.: Myomectomy During the Puerperal State. *Rev. franç. de gynéc. et d'obst.* 22: 421, 1927.

The author reports a series of 56 cases in which myomectomy was performed by various operators during pregnancy and in 41 cases the latter continued after the operation. He also reports five cases in which myomectomy was done after emptying the uterus by cesarean section and four cases in which this operation was resorted to during the puerperium. His conclusions are as follows: Surgical intervention is seldom necessary during pregnancy and when indicated, myomectomy can frequently be done in the early months of gestation without interfering with the further evolution of the ovum. During the latter months of pregnancy, operation is rarely necessary. During labor the chief indication is a fibroid blocking the pelvis and enucleation can be performed after cesarean section. During the puerperium, an operation may be made imperative because of hemorrhage and pain. A hysterectomy is to be performed at the end of pregnancy if there are multiple fibroids, or incarcerated ones, during labor if the tumors are multiple and during the puerperium if infection is feared.

J. P. GREENHILL.

Vandescal, R.: Myomectomy During Pregnancy. *British M. J.* 2: 793, 1928.

In general myomectomy during pregnancy is contraindicated because it leaves a weak scar in the uterine wall.

Myomectomy is permissible in the following conditions: (1) When the fibroid is large and diagnosed early (before third month) and when the tumor can be dif-

ferentiated from the uterus. (2) At any time when necrobiosis of the tumor is demonstrable by such symptoms as pain, softening of the tumor or peritoneal irritation. (3) When there is a torsion of the pedicle with peritoneal irritation. (4) When there is a retroversion due to the tumor and (5) when pressure by tumor leads to hydronephrosis, venous stasis, etc.

The following technic is advised for operations: (1) General anesthesia is preferable. (2) Decapsulate the tumor by an incision around its summit and not around the base. (3) Stop all bleeding carefully. (4) Use no drainage. (5) Give morphine in large doses.

In following the above conditions the clinic has had 1.9 per cent maternal and 13.0 per cent fetal mortality.

ADAIR-HESDORFER.

Gaudier, H., and Bournoville, L.: Escape of Liquor Amnii During a Myomectomy on a Four Months' Pregnant Uterus. Continuation of Pregnancy Until the Seventh Month. *Bull. Soc. d'obst. et de gynec.* 16: 516, 1927.

A thirty-nine year old primipara complained of severe abdominal pain. Bimanual examination revealed a fibroid uterus the size of a four months' pregnancy. A laparotomy was performed and a pregnant uterus with large myomas found. Two large myomas were removed and when the second one was enucleated the bag of waters was unintentionally ruptured. A fetal small part presented itself in the wound, and before it was closed, practically all the amniotic fluid had escaped. The patient was given opium and made an uneventful recovery. Before discharge from the hospital there was noticed a return of liquor amnii in the uterus. The patient had a premature labor in the seventh month but the child died during labor. There was no evidence of a scar in the membranes.

J. P. GREENHILL.

P. Nubiola, and V. Carulla: Intraabdominal Curie-therapy in Cancer of the Cervix and Pregnancy. *Rev. espan. de obst. y ginec.* 11: 1, 1926.

The authors report the case of a woman at term treated by abdominal cesarean, extensive hysterectomy, and the placing, via the abdominal route, of four tubes, each containing 6.50 mg. of radium, in the regions most involved by the cancerous process. In this way 22 millicuries were administered in 120 hours, combined with a dosage of 18.8 millicuries applied in nine days through the vagina. Deep roentgen radiation was used as a complementary treatment. The result was good for six months of postoperative observation.

Superficial radium treatment of cervical cancer is indicated in pregnancy where the fetus is not yet viable, but deep treatment may cause abortion. X-ray treatment is contraindicated during pregnancy. When the fetus is viable operative treatment should precede radium therapy, as otherwise peritoneal infection may follow operation. In such cases the widest possible hysterectomy should be done in order to facilitate the application and action of radium, which, as the above case shows, is well tolerated and is most effective if applied intraabdominally. Subsequently x-ray treatment should be used against possible recurrence.

THOS. R. GOETHALS.

Schockaert: Cervical Cancer and Pregnancy. *Bruxelles-med.* 7: 15, 1926.

Schockaert believes that cancer of the cervix complicated by pregnancy is rare because the majority of cervical cancers appear during the fourth decade of life, at which time pregnancy is less apt to occur. While the malignant growth may originate in a uterus already pregnant, the author believes that the reverse is the more common occurrence. The treatment of these cases depends upon whether or



not the malignancy is operable. In the first instance only the life of the mother should be taken into consideration. When, however, metastases have developed, the tumor should be treated conservatively in an effort to carry the fetus past the point of viability. Schoekaert feels that irradiation of these cases would almost invariably cause abortion.

The case of a woman thirty years of age is reported. At the time she was first seen the pregnancy had advanced to two and one-half months. She gave a history of a watery, foul smelling discharge for a longer period, so in all probability the malignancy antedated the pregnancy. A radical Wertheim with resection of the iliac glands was done. Sufficient time had not elapsed to state the ultimate outcome.

THEODORE W. ADAMS.

**Karg, C.: Pregnancy After and in the Presence of Cancer of the Uterus.** *Monatschr. f. Geburtsh. u. Gynäk.* 78: 264, 1928.

The author collected from the literature six cases in which pregnancy followed the occurrence of carcinoma of the cervix. All of the patients were treated by radiation and in three cases spontaneous delivery afterward took place. He found two additional cases of pregnancy occurring after carcinoma of the vulva. All of the children born were entirely normal, hence, the author agrees with Schmitt, Nürnberger and others that children born after a period of amenorrhea produced by radium or roentgen rays show no defects. The author also collected from the literature ten cases where pregnancy occurred in the presence of carcinoma of the uterus and he adds two cases. All of the patients were treated with radium. In nine cases there was a spontaneous delivery, in one a vaginal cesarean section and in two instances an abortion. All the children born were normal. The author believes that cancer of the uterus during pregnancy should be treated with radium because it not only preserves the life of the mother as well as operation but also saves the life of the baby.

J. P. GREENHILL.

**Roy: A Few Cases of Cervico-Uterine Epithelioma in Pregnant Women Treated With Radium.** *Bullet. Soc. d'obst. et de gynéc.* 17: 653, 1928.

The author reports four cases of carcinoma of the cervix encountered during pregnancy. Three of the patients were treated with radium during the latter months of pregnancy and the fourth received treatment one month after a cesarean section was performed. Three patients were delivered by cesarean section and one had a spontaneous delivery at the seventh month. Two patients died, one was in good health two years after delivery and one was in good health one month after cesarean section. One child died in utero, one was in good health at two years of age, one was normal at fifteen days and the last appeared normal at one month of age.

J. P. GREENHILL.

## Item

### An American Board of Obstetrics and Gynecology

A BRIEF RÉSUMÉ OF THE PROGRESS MADE TO OCTOBER 1, 1929, IN ITS CREATION AND ORGANIZATION

I. At the meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons held in Asheville, N. C., September 15 to 17, 1927, Dr. Walter T. Dannreuther of New York introduced a preamble and resolution providing for the appointment of a committee on standardization of requirements for specialists in obstetrics and gynecology, and suggesting the appointment of a similar committee by the American Gynecological Society. The primary function of this committee was to consider ways and means for the organization of an American Board of Obstetrics and Gynecology. This resolution was reported on favorably by the Council and unanimously adopted. Dr. John O. Polak, President, appointed the following committee:

Dr. Walter T. Dannreuther,	New York, Chairman
Dr. Louis E. Phaneuf,	Boston
Dr. Arthur H. Bill,	Cleveland
Dr. Frederick H. Falls,	Chicago
Dr. Grandison D. Royston,	St. Louis

II. A communication was sent from the American Association of Obstetricians, Gynecologists and Abdominal Surgeons to the American Gynecological Society suggesting the appointment of a committee by the latter organization to cooperate and act jointly with the existing committee. The American Gynecological Society, at its next meeting in May, 1928, named:

Dr. Jennings C. Litzenberg,	Minneapolis, Chairman
Dr. Louis Baer,	Chicago
Dr. Herbert M. Little,	Montreal
Dr. Edmond D. Piper,	Philadelphia
Dr. Edward A. Schumann,	Philadelphia

III. A meeting of the committee representing the American Association of Obstetricians, Gynecologists and Abdominal Surgeons was held just prior to the Association's meeting in Toronto, September 10 to 12, 1928. Dr. Litzenberg was present by invitation and participated in the discussions and formulation of a plan for the organization of an American Board of Obstetrics and Gynecology. This plan provided for the appointment for five years of nine examiners, three to be appointed by the American Association of Obstetricians, Gynecologists and Abdominal Surgeons; three by the American Gynecological Society, and three by the Section on Obstetrics, Gynecology and Abdominal Surgery of the American Medical Association. The Committee's formal report included a brief statement of the purposes of the Board, the general requirements for all applicants and the classification of applicants. It provided for the examination of voluntary candidates and the issuance of certificates to the successful applicants and expressed the hope that all well-established gynecologists and obstetricians will apply for the certificate of the Board.

A recommendation was made that a copy of the report be forwarded to the American Gynecological Society and another to the Section on Obstetrics, Gynecology and Abdominal Surgery of the American Medical Association with a request that a committee be appointed by the American Medical Association Section to cooperate with the two existing committees.

IV. After the meeting of the American Gynecological Society in May, 1929, Dr. Litzenberg wrote to the Chairman of the Committee of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons stating that the American Gynecological Society was willing to cooperate in any plan feasible for the principle proposed in the original resolution.

V. Dr. Walter T. Dannreuther of New York introduced a preamble and resolution at the meeting of the Section on Obstetrics, Gynecology and Abdominal Surgery of the American Medical Association at its meeting in Portland, Oregon, in July, 1929, committing the Section to participate in the organization of an American Board of Obstetrics and Gynecology. The resolution was adopted and the newly elected Chairman of the Section was authorized to appoint a committee of three to cooperate with the two existing committees.

VI. At the meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons held in Memphis, Tenn., September 16 to 18, 1929, the Committee on Standardization of Requirements for Specialists in Obstetrics and Gynecology filed a report referring to the following important items:

a. Reprinting of the Committee's 1928 report in the *Journal of the American Medical Association*, November 24, 1928.

b. Favorable editorial comment on the project in the *Journal of the American Medical Association*, January 5, 1929.

c. Pertinent editorial articles in the *New York Medical Weekly*, February 23, 1929, and the *New England Medical Journal*, February 2, 1929.

d. Comments of Dr. Harry R. Trick, President of the Medical Society of the State of New York in his report to the House of Delegates.

e. Memorization of the Board of Regents of the State of New York by the House of Delegates that some action be taken for the legal certification of specialists.

f. The recent organization of the British College of Obstetrics and Gynecology.

g. The receipt of several applications for the certificates of the Board.

h. Recommendations that three fellows of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons be elected to serve as representatives and examiners on the American Board of Obstetrics and Gynecology.

VII. The American Association of Obstetricians, Gynecologists and Abdominal Surgeons thereupon elected Dr. Walter T. Dannreuther of New York, N. Y., Dr. Paul Titus, Pittsburgh, and Dr. Grandison D. Royston, St. Louis, to serve for five years as its representatives and examiners on the American Board of Obstetrics and Gynecology.

VIII. As soon as the American Gynecological Society and the Section on Obstetrics, Gynecology and Abdominal Surgery of the American Medical Association each elect their three representatives and examiners the Board can be organized and begin to function.

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